SEARCH REQUEST FORM 281969

Earliest Priority Date:

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only: Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

See claims attached. Please do structure search and inventor name(s) search. Display results to show identification of source, and RN#, compound name & structure of identified compounds. Search Compounds of Formula I as indicated.

Please call with any questions.

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Searcher:

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up:

Date Completed:

Searcher Prep & Review Time:

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Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#)

Bibliographic

Litigation

Fulltext

Other

Vendors and cost where applicable

STN

Dialog

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Lexis/Nexis

Westlaw

WWW/Internet

In-house sequence systems

Commercial

Litigation

Interference

SPDI

Other (specify)

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L1            1 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS


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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y



L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2005:523430  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:60003
TITLE:                    Preparation of 6-substituted 2-quinolinones and
                          2-quinoxalinones as poly(ADP-ribose) polymerase
                          inhibitors
INVENTOR(S):              Mabire, Dominique Jean-Pierre; Guillemont, Jerome
                          Emile Georges; Van Dun, Jacobus Alphonsus Josephus;
                          Somers, Maria Victorina Francisca; Wouters, Walter
                          Boudewijn Leopold
PATENT ASSIGNEE(S):       Janssen Pharmaceutica N. V., Belg.
SOURCE:                   PCT Int. Appl., 48 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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     WO 2005054210        A1    20050616    WO 2004-EP13164          20041118
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
             SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     AU 2004295059        A1    20050616    AU 2004-295059           20041118
     CA 2546657           A1    20050616    CA 2004-2546657          20041118
     EP 1709012           A1    20061011    EP 2004-819602           20041118
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
             HR, IS, YU
     CN 1890224           A     20070103    CN 2004-80035857         20041118
     BR 2004016532        A     20070109    BR 2004-16532            20041118
     JP 2007513101        T     20070524    JP 2006-541830           20041118
     IN 2006DN03071       A     20070810    IN 2006-DN3071           20060529
     US 20070129375       A1    20070607    US 2006-596086           20060530 <--
     MX 2006PA06255       A     20060809    MX 2006-PA6255           20060602
     NO 2006003028        A     20060628    NO 2006-3028             20060628
PRIORITY APPLN. INFO.:                       EP 2003-78859        A  20031205
                                             WO 2004-EP13164      W  20041118
OTHER SOURCE(S):          CASREACT 143:60003; MARPAT 143:60003
ED   Entered STN:  17 Jun 2005
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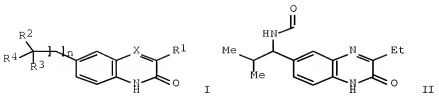
GI



I II

AB The title compds. I [n = 0-2; X = N, CR5; R5 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thienyl; R2 = H, OH, or taken together with R3 or R4 may form O; R3 = OH, OR8, SR9, etc.; R8 = alkyl, alkylcarbonyl, dialkylaminoalkyl; R9 = dialkylaminoalkyl; R4 = H, alkyl, furanyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from 1-(4-amino-3-nitrophenyl)-2-methyl-1-propanone, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IC ICM C07D241-44
ICS C07D407-06; C07D401-12; C07D409-14; A61K031-498; A61P043-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST quinolinone prepn PARP polyADPribose polymerase inhibitor; quinoxalinone prepn PARP polyADPribose polymerase inhibitor

IT Combination chemotherapy
Human
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 58319-92-9, Poly(ADP-ribose) polymerase-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 854523-79-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 854523-77-6P 854523-78-7P 854523-80-1P 854523-81-2P 854523-82-3P
854523-83-4P 854523-84-5P 854523-85-6P 854523-86-7P 854523-87-8P
854523-88-9P 854523-89-0P 854523-90-3P 854523-91-4P 854523-92-5P
854523-93-6P 854523-94-7P 854523-95-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 130346-59-7 130346-65-5 130347-67-0 130347-77-2 130347-78-3
130347-79-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)
IT 97-96-1, 2-Ethylbutanal 103-63-9, (2-Bromoethyl)benzene 2217-31-4, 3-Ethyl-2(1H)-quinolinone 15933-07-0, Ethyl 2-oxobutanoate 52395-27-4 73461-22-0 113092-96-9 409346-71-0 409346-80-1, 3-Methyl-6-quinolinecarboxaldehyde 854524-09-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)
IT 854523-96-9P 854523-97-0P 854523-98-1P 854523-99-2P 854524-01-9P 854524-02-0P 854524-03-1P 854524-04-2P 854524-05-3P 854524-06-4P 854524-07-5P 854524-08-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 1 SEA FILE=WPIX SPE=ON ABB=ON PLU=ON L2 NOT AMUSEMENT/TI

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L3 ANSWER 1 OF 1 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2005-435349 [44] WPIX
DOC. NO. CPI: C2005-133554 [44]
TITLE: New 2-quinolinone and 2-quinoxalinone compounds are poly(ADP-ribose) polymerase-1 inhibitors used for treating tissue damage, neurological disorders and vascular stroke
DERWENT CLASS: B02
INVENTOR: GUILLEMONT J E G; MABIRE D J; SOMERS M V F; VAN DUN J A J; VANDUN J A J; WOUTERS W B L; MABIRE D J P
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV; (GUIL-I) GUILLEMONT J E G; (MABI-I) MABIRE D J; (SOME-I) SOMERS M V F; (VDUN-I) VAN DUN J A J; (WOUT-I) WOUTERS W B L
COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005054210	A1	20050616	(200544)*	EN	48[0]	
NO 2006003028	A	20060628	(200654)	NO		
EP 1709012	A1	20061011	(200667)	EN		
AU 2004295059	A1	20050616	(200675)	EN		
BR 2004016532	A	20070109	(200707)	PT		
MX 2006006255	A1	20060801	(200707)	ES		
JP 2007513101	W	20070524	(200735)	JA	46	
KR 2006118534	A	20061123	(200735)	KO		
US 20070129375	A1	20070607	(200738)	EN		

CN 1890224	A	20070103 (200740)	ZH	
ZA 2006004549	A	20080430 (200836)	EN	50
IN 2006DN03071	P1	20070810 (200846)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005054210	A1	WO 2004-EP13164	20041118
AU 2004295059	A1	AU 2004-295059	20041118
BR 2004016532	A	BR 2004-16532	20041118
CN 1890224	A	CN 2004-80035857	20041118
EP 1709012	A1	EP 2004-819602	20041118
NO 2006003028	A	WO 2004-EP13164	20041118
EP 1709012	A1	WO 2004-EP13164	20041118
BR 2004016532	A	WO 2004-EP13164	20041118
MX 2006006255	A1	WO 2004-EP13164	20041118
KR 2006118534	A	WO 2004-EP13164	20041118
JP 2007513101	W	WO 2004-EP13164	20041118
US 20070129375	A1	WO 2004-EP13164	20041118
JP 2007513101	W	JP 2006-541830	20041118
US 20070129375	A1	US 2006-596086	20060530
MX 2006006255	A1	MX 2006-6255	20060602
ZA 2006004549	A	ZA 2006-4549	20060602
KR 2006118534	A	KR 2006-711234	20060608
NO 2006003028	A	NO 2006-3028	20060628
IN 2006DN03071	P1	WO 2004-EP13164	20041118
IN 2006DN03071	P1	IN 2006-DN3071	20060529

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1709012	A1	Based on	WO 2005054210	A
AU 2004295059	A1	Based on	WO 2005054210	A
MX 2006006255	A1	Based on	WO 2005054210	A
BR 2004016532	A	Based on	WO 2005054210	A
KR 2006118534	A	Based on	WO 2005054210	A
JP 2007513101	W	Based on	WO 2005054210	A

PRIORITY APPLN. INFO: EP 2003-78859 20031205

INT. PATENT CLASSIF.:

MAIN:	A61K031-498; C07D; C07D241-44
SECONDARY:	A61K; A61P; A61P043-00; C07D401-12; C07D407-06; C07D409-14
IPC ORIGINAL:	A61K0031-4704 [I,A]; A61K0031-4704 [I,C]; A61K0031-4709 [I,C]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61K0031-472 [I,C]; A61K0031-4725 [I,A]; A61K0031-473 [I,A]; A61K0031-473 [I,C]; A61K0031-498 [I,A]; A61K0031-498 [I,C]; A61K0031-498 [I,A]; A61K0031-498 [I,C]; A61K0031-498 [I,A]; A61K0031-498 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0017-00 [I,C]; A61P0017-02 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0019-10 [I,A]; A61P0021-00 [I,A]; A61P0021-00 [I,C]; A61P0021-04 [I,A]; A61P0025-00 [I,C]; A61P0025-14 [I,A]; A61P0025-16 [I,A]; A61P0025-22 [I,A]; A61P0025-28 [I,A]; A61P0025-30 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0037-00 [I,A]; A61P0037-00 [I,C]; A61P0037-04 [I,A];

A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0043-00 [I,A];
A61P0043-00 [I,C]; A61P0009-00 [I,C]; A61P0009-10 [I,A];
C07D0215-00 [I,C]; C07D0215-00 [I,C]; C07D0215-22 [I,A];
C07D0215-227 [I,A]; C07D0241-00 [I,C]; C07D0241-00 [I,C];
C07D0241-00 [I,C]; C07D0241-00 [I,C]; C07D0241-36 [I,A];
C07D0241-44 [I,A]; C07D0241-44 [I,A]; C07D0241-44 [I,A];
C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C];
C07D0401-06 [I,A]; C07D0401-12 [I,A]; C07D0401-12 [I,A];
C07D0401-12 [I,A]; C07D0405-00 [I,C]; C07D0405-06 [I,A];
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C07D0409-14 [I,A]; C07D0409-14 [I,A]; C07D0409-14 [I,A]

IPC RECLASSIF.: C07D0241-00 [I,C]; C07D0241-44 [I,A]; C07D0401-00 [I,C];
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ECLA: C04B0035-632; C07D0241-44; C07D0401-12; C07D0407-06;
C07D0409-14

ICO: M07D0241:44

USCLASS NCLM: 514/249.000

NCLS: 514/290.000; 514/312.000; 544/353.000; 546/079.000;
546/157.000

JAP. PATENT CLASSIF.:

MAIN/SEC.: A61K0031-4704; A61K0031-4709; A61K0031-4725;
A61K0031-498; A61K0045-00; A61P0001-04; A61P0017-02;
A61P0019-02; A61P0019-10; A61P0021-00; A61P0021-04;
A61P0025-14; A61P0025-16; A61P0025-22; A61P0025-28;
A61P0025-30; A61P0029-00; A61P0003-10; A61P0035-00;
A61P0037-00; A61P0037-04; A61P0043-00 105; A61P0043-00
111; A61P0009-10; A61P0009-10 101; C07D0215-22;
C07D0401-06; C07D0401-12; C07D0405-06; C07D0409-14;
C07D0241-44 (CSP)

FTERM CLASSIF.: 4C031; 4C044; 4C063; 4C084; 4C086; 4C201; 4C063/AA01;
4C086/AA01; 4C086/AA02; 4C063/AA03; 4C086/AA03;
4C084/AA19; 4C063/BB03; 4C063/BB09; 4C086/BC28;
4C086/BC38; 4C086/BC52; 4C086/BC60; 4C063/CC14;
4C063/CC25; 4C063/CC75; 4C063/CC92; 4C063/DD10;
4C063/DD12; 4C063/DD14; 4C063/DD34; 4C031/EA06;
4C031/EA08; 4C031/EA09; 4C063/EE01; 4C086/GA02;
4C086/GA04; 4C086/GA07; 4C086/GA08; 4C086/MA01;
4C084/MA02; 4C086/MA04; 4C084/NA14; 4C086/NA14;
4C084/ZA02.2; 4C086/ZA02; 4C084/ZA05.2; 4C086/ZA05;
4C084/ZA08.2; 4C086/ZA08; 4C084/ZA16.2; 4C086/ZA16;
4C084/ZA18.2; 4C086/ZA18; 4C084/ZA36.2; 4C086/ZA36;
4C084/ZA45.2; 4C086/ZA45; 4C084/ZA68.2; 4C086/ZA68;
4C084/ZA89.2; 4C086/ZA89; 4C084/ZA94.2; 4C086/ZA94;
4C084/ZA96.2; 4C086/ZA96; 4C084/ZA97.2; 4C086/ZA97;
4C084/ZB07.2; 4C086/ZB07; 4C084/ZB09.2; 4C086/ZB09;
4C084/ZB21.2; 4C086/ZB21; 4C084/ZB26.2; 4C086/ZB26;
4C084/ZC02.2; 4C086/ZC02; 4C084/ZC35.2; 4C086/ZC35;
4C084/ZC39.2; 4C086/ZC39

BASIC ABSTRACT:

WO 2005054210 A1 UPAB: 20051222

NOVELTY - 2-Quinolinone and 2-quinoxalinone compounds (I), are new.

DETAILED DESCRIPTION - 2-Quinolinone and 2-quinoxalinone compounds of formula (I), their N-oxides, salts and isomers, are new.

n = 0-2;

X = N or CR5;

R1 = 1-6C alkyl or thienyl;

R5 = H, or

R5 + R1 = CH=CH-CH=CH;

R2 = H or hydroxy;
R3 = (CH2)s-NR6R7, OH, O-R8, S-R9, CN or Z;
R4 = H, 1-6C alkyl, furanyl, pyridinyl or aryl 1-6C alkyl, or
R2 + R3 or R4 = =O;
s = 0-3;
R6 = CHO, 1-6C alkyl, hydroxy 1-6C alkyl, 1-6C alkylcarbonyl, di(1-6C alkyl)amino 1-6C alkyl, 1-6C alkyloxy 1-6C alkyl, 1-6C alkylcarbonylamino 1-6C alkyl, piperidinyl 1-6C alkylaminocarbonyl, piperidinyl, piperidinyl 1-6C alkyl, piperidinyl 1-6C alkylaminocarbonyl, 1-6C alkyloxy, thienyl 1-6C alkyl, pyrrolyl 1-6C alkyl, aryl 1-6C alkylpiperidinyl, arylcarbonyl 1-6C alkyl, arylcarbonylpiperidinyl 1-6C alkyl, haloindozolylpiperidinyl 1-6C alkyl, or aryl 1-6C alkyl(1-6C alkyl)amino 1-6C alkyl;
R7 = H or 1-6C alkyl;
R8 = 1-6C alkyl, 1-6C alkylcarbonyl or di(1-6C alkyl)amino 1-6C alkyl;
R9 = di(1-6C alkyl)amino 1-6C alkyl;
Z = a group of formula (c-1)-(c-6);
R10 = H, 1-6C alkyl, aminocarbonyl, hydroxy, 1-6C alkyloxy 1-6C alkyl, 1-6C alkyloxy 1-6C alkyl amino, aryl 1-6C alkyl, di(phenyl 2-6C alkenyl), piperidinyl 1-6C alkyl, 3-10C cycloalkyl, 3-10C cycloalkyl 1-6C alkyl, aryloxy(hydroxy)1-6C alkyl, haloindazolyl, aryl 1-6C alkyl, aryl 2-6C alkenyl, morpholino, 1-6C alkylimidazolyl, pyridinyl 1-6C alkylamino or a group of formula (i) or (ii), and
aryl = phenyl optionally substituted by halo, 1-6C alkyl or 1-6C alkyloxy,
provided that when n is 0, X is N, R2 is H, R3 is (c-2) or (c-4) and R10 is H, then R4 is not 1-6C alkyl or pyridinyl.

INDEPENDENT CLAIMS are also included for:
(1) a composition which comprises compound (I) and carriers;
(2) preparation of the composition which comprises mixing compound (I) and carriers;
(3) a combination of compound (I) with chemotherapeutic agent; and
(4) preparation of (I).

ACTIVITY - Neuroprotective; Vasotropic; Cerebroprotective; Cardiovascular-Gen.; Muscular-Gen.; Anti-HIV; Immunosuppressive; Antiinflammatory; Antigout; Antiarthritic; Antiarteriosclerotic; Immunomodulator; Cytostatic; Antidiabetic; Vulnerary; Gastrointestinal-Gen.; Osteopathic; Analgesic; Nephrotropic; Ophthalmological; Antibacterial; Dermatological.

MECHANISM OF ACTION - Poly(ADP-ribose) polymerase-1 (PPAR-1) inhibitor.

In an in vitro scintillation proximity assay using nicked DNA activated PPAR-1 enzyme, results showed that 6-(1-(1H-imidazol-1-yl)pentyl)-3-methyl-2(1H)-quinoxalinone exhibited a pIC50 value of 6 for inhibiting PPAR-1.

USE - Used for the treatment of PARP mediated disorder by chemosensitization and radiosensitization (claimed), particularly tissue damage, neurological disorders, vascular stroke, cardiovascular disorder, age-related macular degeneration, AIDS, immune diseases, inflammation, gout, arthritis, atherosclerosis, cachexia, cancer, degenerative diseases of skeletal muscle, diabetes, head trauma, inflammatory bowel disorders, muscular dystrophy, osteoarthritis, osteoporosis, pain, renal failure, retinal ischemia, septic shock and skin aging. MANUAL CODE: CPI: B06-D02; B06-D06; B06-D13; B14-A02B1; B14-C01; B14-C02; B14-C03; B14-C09; B14-C09A; B14-D03; B14-E10C1; B14-E11B; B14-F01; B14-F02; B14-F02D; B14-F02D1; B14-F07; B14-G01B; B14-G03; B14-H01; B14-J01; B14-J05; B14-N01; B14-N03; B14-N10; B14-N16; B14-N17; B14-N17B; B14-S04; B14-S06

AN 2005-435349 [44] WPIX
DC B02
IC ICM A61K031-498; C07D; C07D241-44
ICS A61K; A61P; A61P043-00; C07D401-12; C07D407-06; C07D409-14

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NCL NCLM 514/249.000
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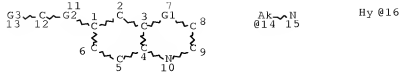


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LAST RELOADED: Dec 19, 2008 (20081219/UP).

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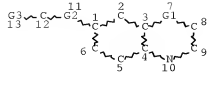

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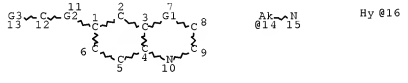


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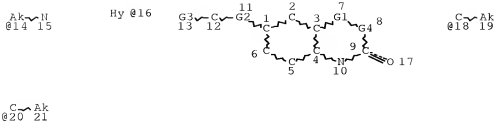

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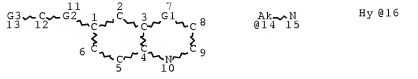

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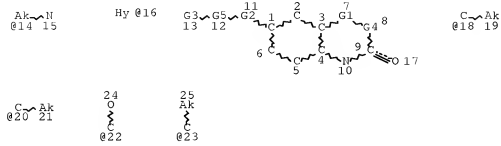
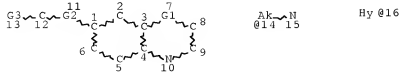
ECOUNT IS X4 C AT 14
ECOUNT IS M2-X3 C M2-X3 N E0 O E0 P E0 S E0 Si AT 16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

```
STEREO ATTRIBUTES: NONE
L8   (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                  NC2NC2-C6/ES
L9         22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L21               STR
```

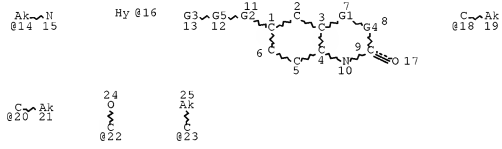



```
VAR G1=N/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L23        1824 SEA FILE=REGISTRY SUB=L9 SSS FUL L21

100.0% PROCESSED    5339 ITERATIONS                          1824 ANSWERS
SEARCH TIME: 00.00.01


=> d que stat l37
L7                STR
```

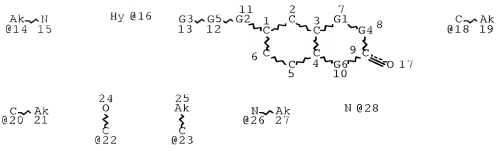



```
VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
```

```
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L8  (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L9        22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L21             STR
```




```
VAR G1=N/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L23         1824 SEA FILE=REGISTRY SUB=L9 SSS FUL L21
L34              STR
```




```
VAR G1=28/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC   IS R      AT  28
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  27
CONNECT IS E2  RC AT  28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L37        1447 SEA FILE=REGISTRY SUB=L23 SSS FUL L34

100.0% PROCESSED    1824 ITERATIONS                          1447 ANSWERS
SEARCH TIME: 00.00.01


=> d his ful

     (FILE 'HOME' ENTERED AT 14:53:30 ON 07 JAN 2009)

     FILE 'STNGUIDE' ENTERED AT 14:53:33 ON 07 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 14:54:11 ON 07 JAN 2009
               ACT JAI086HCAAPP/A
               ---------
L1           1 SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
               ---------

     FILE 'WPIX' ENTERED AT 14:54:33 ON 07 JAN 2009
               ACT JAI086WPIAPP/A
```

```
                 ---------
L2  (          2)SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
L3             1 SEA SPE=ON  ABB=ON  PLU=ON  L2 NOT AMUSEMENT/TI
                 ---------


     FILE 'REGISTRY' ENTERED AT 14:54:42 ON 07 JAN 2009
                 ACT JAI086REGAPP/A
                 ---------
L4  (          1)SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
L5               SEL PLU=ON  L4 1- RN :       48 TERMS
L6            48 SEA SPE=ON  ABB=ON  PLU=ON  L5
                 ---------
                 ACT JAI086PSET1/A
                 ---------
L7               STR
L8  (    1332204)SEA SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR NC2NC2-C6/ES
L9         22147 SEA SUB=L8 SSS FUL L7
                 ---------

     FILE 'LREGISTRY' ENTERED AT 14:55:32 ON 07 JAN 2009
L10              STR L7

     FILE 'REGISTRY' ENTERED AT 14:55:49 ON 07 JAN 2009
L11           50 SEA SUB=L9 SSS SAM L10

     FILE 'LREGISTRY' ENTERED AT 14:56:19 ON 07 JAN 2009
L12              STR L10

     FILE 'REGISTRY' ENTERED AT 14:57:25 ON 07 JAN 2009
L13            8 SEA SSS SAM L12

     FILE 'LREGISTRY' ENTERED AT 14:57:50 ON 07 JAN 2009
L14              STR L12

     FILE 'REGISTRY' ENTERED AT 14:58:28 ON 07 JAN 2009
L15           50 SEA SUB=L9 SSS SAM L14

     FILE 'STNGUIDE' ENTERED AT 14:59:18 ON 07 JAN 2009
                 D QUE STAT

     FILE 'REGISTRY' ENTERED AT 15:06:12 ON 07 JAN 2009
L16         1904 SEA SUB=L9 SSS FUL L14
                 SAVE TEMP L16 JAI086RSET1/A
L17           26 SEA SPE=ON  ABB=ON  PLU=ON  L6 NOT L9
L*** DEL      12 S L17 NOT (NC5/ESS OR NC3NC2/ESS)
L18            9 SEA SPE=ON  ABB=ON  PLU=ON  L17 NOT (NC5/ESS OR NC2NC2/ESS)
L19           17 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND (NC5/ESS OR NC2NC2/ESS)
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 15:09:18 ON 07 JAN 2009
                 D SAVED

     FILE 'HCAPLUS' ENTERED AT 15:09:50 ON 07 JAN 2009
L20           174 SEA SPE=ON  ABB=ON  PLU=ON  L16

     FILE 'STNGUIDE' ENTERED AT 15:10:07 ON 07 JAN 2009

     FILE 'LREGISTRY' ENTERED AT 15:10:46 ON 07 JAN 2009
L21              STR L14
```

```
     FILE 'REGISTRY' ENTERED AT 15:12:26 ON 07 JAN 2009
L22           50 SEA SUB=L9 SSS SAM L21
L*** DEL          STR L21

     FILE 'STNGUIDE' ENTERED AT 15:14:33 ON 07 JAN 2009
                D QUE L22 STAT

     FILE 'REGISTRY' ENTERED AT 15:15:56 ON 07 JAN 2009
L23         1824 SEA SUB=L9 SSS FUL L21
                SAVE TEMP L23 JAI086RSET2/A

     FILE 'STNGUIDE' ENTERED AT 15:16:48 ON 07 JAN 2009
                D SAVED

     FILE 'REGISTRY' ENTERED AT 15:17:10 ON 07 JAN 2009
L24         1824 SEA SPE=ON  ABB=ON  PLU=ON  L16 AND L23
L25           31 SEA SPE=ON  ABB=ON  PLU=ON  L6 NOT L24
L26           22 SEA SPE=ON  ABB=ON  PLU=ON  L25 NOT L18
L27            5 SEA SPE=ON  ABB=ON  PLU=ON  L26 NOT L19
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 15:19:27 ON 07 JAN 2009

     FILE 'REGISTRY' ENTERED AT 15:19:55 ON 07 JAN 2009
L28           31 SEA SPE=ON  ABB=ON  PLU=ON  L6 NOT L24
L29           22 SEA SPE=ON  ABB=ON  PLU=ON  L28 AND (NC5/ESS OR NC2NC2/ESS)
L30            5 SEA SPE=ON  ABB=ON  PLU=ON  L29 NOT L19
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 15:21:15 ON 07 JAN 2009
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 15:22:40 ON 07 JAN 2009
L31          148 SEA SPE=ON  ABB=ON  PLU=ON  L23

     FILE 'LREGISTRY' ENTERED AT 15:23:27 ON 07 JAN 2009
L32             STR L21

     FILE 'REGISTRY' ENTERED AT 15:32:33 ON 07 JAN 2009
L33           50 SEA SUB=L23 SSS SAM L32

     FILE 'LREGISTRY' ENTERED AT 15:33:30 ON 07 JAN 2009
L34             STR L32

     FILE 'STNGUIDE' ENTERED AT 15:36:04 ON 07 JAN 2009

     FILE 'REGISTRY' ENTERED AT 15:49:03 ON 07 JAN 2009
L35           50 SEA SUB=L23 SSS SAM L34

     FILE 'STNGUIDE' ENTERED AT 15:49:18 ON 07 JAN 2009
                D QUE STAT

     FILE 'REGISTRY' ENTERED AT 15:52:24 ON 07 JAN 2009
L36           50 SEA SUB=L23 SSS SAM L34
L37         1447 SEA SUB=L23 SSS FUL L34
                SAVE TEMP L37 JAI086RSET3/A

     FILE 'STNGUIDE' ENTERED AT 15:53:52 ON 07 JAN 2009
                D SAVED
```

```
     FILE 'STNGUIDE' ENTERED AT 15:55:00 ON 07 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 15:55:30 ON 07 JAN 2009
                ACT JAI086HCAAPP/A
                ---------
L*** DEL       1 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
                ---------

     FILE 'WPIX' ENTERED AT 15:55:43 ON 07 JAN 2009
                ACT JAI086WPIAPP/A
                ---------
L***(DEL       2)SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
L*** DEL       1 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L39 NOT AMUSEMENT/TI
                ---------

     FILE 'STNGUIDE' ENTERED AT 15:56:01 ON 07 JAN 2009

     FILE 'REGISTRY' ENTERED AT 15:56:38 ON 07 JAN 2009

     FILE 'STNGUIDE' ENTERED AT 15:58:07 ON 07 JAN 2009
                D SAVED

     FILE 'STNGUIDE' ENTERED AT 16:19:10 ON 07 JAN 2009

     FILE 'REGISTRY' ENTERED AT 16:19:20 ON 07 JAN 2009
L38           17 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L37

     FILE 'HCAPLUS' ENTERED AT 16:20:04 ON 07 JAN 2009
L39          128 SEA SPE=ON  ABB=ON  PLU=ON  L37

     FILE 'STNGUIDE' ENTERED AT 16:20:22 ON 07 JAN 2009
                D QUE STAT L9
                D QUE STAT L16
                D QUE STAT L23
                D QUE STAT L37


     FILE HOME

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
     LAST RELOADED: Jan  6, 2009 (20090106/UP).

     FILE HCAPLUS

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     FILE COVERS 1907 - 7 Jan 2009  VOL 150 ISS 2
     FILE LAST UPDATED: 6 Jan 2009  (20090106/ED)

     HCAplus now includes complete International Patent Classification (IPC)
     reclassification data for the third quarter of 2008.
```

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FILE LAST UPDATED: 3 JAN 2009 <20090103/UP>
MOST RECENT UPDATE: 200901 <200901/DW>
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ECLA reclassifications to mid August and US national classification mid September 2008 have also been loaded. Update dates 20080401, 20080701 and 20081001/UPEC and /UPNC have been assigned to these. <<

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>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JAN 2009 HIGHEST RN 1092767-60-6
DICTIONARY FILE UPDATES: 6 JAN 2009 HIGHEST RN 1092767-60-6

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http://www.cas.org/support/stngen/stndoc/properties.html

FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

```
=> => d que stat 19
L7              STR
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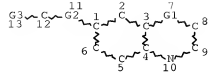


```
VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L8  (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L9        22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7

100.0% PROCESSED  417169 ITERATIONS                          22147 ANSWERS
SEARCH TIME: 00.00.04


=> d que stat l14
L10             STR
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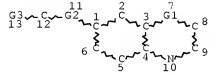
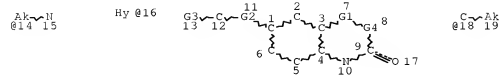
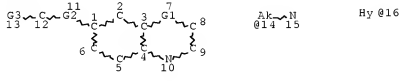



```
VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
```

```
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L11 (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L12 (     22147)SEA FILE=REGISTRY SUB=L11 SSS FUL L10
L13             STR
```

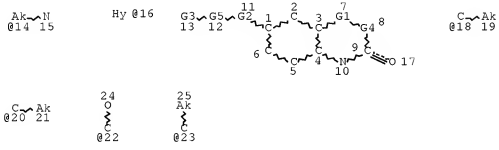



```
VAR G1=N/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L14        1904 SEA FILE=REGISTRY SUB=L12 SSS FUL L13

100.0% PROCESSED    5339 ITERATIONS                          1904 ANSWERS
SEARCH TIME: 00.00.01


=> d que stat l19
L15             STR
```

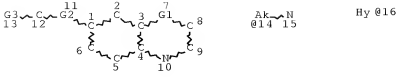



```
VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
```

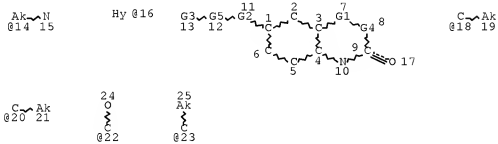
```
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L16 (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L17 (     22147)SEA FILE=REGISTRY SUB=L16 SSS FUL L15
L18             STR
```




```
VAR G1=N/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L19        1824 SEA FILE=REGISTRY SUB=L17 SSS FUL L18

100.0% PROCESSED    5339 ITERATIONS                          1824 ANSWERS
SEARCH TIME: 00.00.01


=> d que stat l26
L20             STR
```

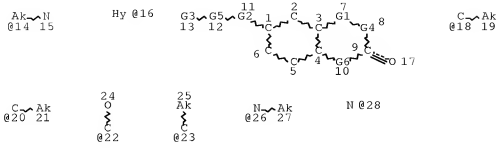


```
VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 N  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L21 (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L22 (     22147)SEA FILE=REGISTRY SUB=L21 SSS FUL L20
L23             STR
```



```
VAR G1=N/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25
```

STEREO ATTRIBUTES: NONE
L24 (1824)SEA FILE=REGISTRY SUB=L22 SSS FUL L23
L25 STR



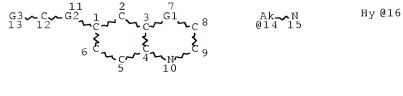
VAR G1=28/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC IS R AT 28
CONNECT IS E2 RC AT 14
CONNECT IS E1 RC AT 19
CONNECT IS E1 RC AT 21
CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 27
CONNECT IS E2 RC AT 28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS X4 C AT 14
ECOUNT IS M2-X3 C M2-X3 N E0 O E0 P E0 S E0 Si AT 16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L26 1447 SEA FILE=REGISTRY SUB=L24 SSS FUL L25

100.0% PROCESSED 1824 ITERATIONS 1447 ANSWERS
SEARCH TIME: 00.00.01

=> d que stat l67
L7 STR



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VAR G1=N/C
REP G2=(0-3) C
VAR G3=N/14/16
NODE ATTRIBUTES:
CONNECT IS E2  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L8  (   1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                NC2NC2-C6/ES
L9         22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L65             STR
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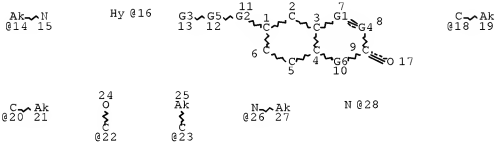


```
VAR G1=28/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC   IS R      AT  28
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  27
CONNECT IS E2  RC AT  28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L67         429 SEA FILE=REGISTRY SUB=L9 SSS FUL L65
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100.0% PROCESSED    5571 ITERATIONS                    429 ANSWERS
SEARCH TIME: 00.00.01


=> d que nos l72
L7                STR
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                  NC2NC2-C6/ES
L9         22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L32               QUE  SPE=ON  ABB=ON  PLU=ON  MABIRE, D?/AU
L33               QUE  SPE=ON  ABB=ON  PLU=ON  GUILLEMONT, J?/AU
L34               QUE  SPE=ON  ABB=ON  PLU=ON  VAN DUN, J?/AU
L35               QUE  SPE=ON  ABB=ON  PLU=ON  VANDUN, J?/AU
L36               QUE  SPE=ON  ABB=ON  PLU=ON  SOMERS, M?/AU
L37               QUE  SPE=ON  ABB=ON  PLU=ON  WOUTERS, W?/AU
L38               QUE  SPE=ON  ABB=ON  PLU=ON  JANSSEN/CS,SO,PA
L65               STR
L67           429 SEA FILE=REGISTRY SUB=L9 SSS FUL L65
L70            45 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L67
L71             6 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L70 AND (L32 OR L33
                  OR L34 OR L35 OR L36 OR L37 OR L38)
L72            39 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L70 NOT L71


=> d que stat l78
L65               STR
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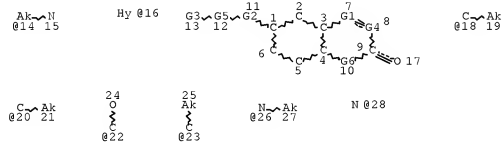


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VAR G1=28/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC   IS R       AT  28
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  27
CONNECT IS E2  RC AT  28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16
```

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L78          16 SEA FILE=WPIX SSS FUL L65

100.0% PROCESSED   92855 ITERATIONS                          16 ANSWERS
SEARCH TIME: 00.00.44


=> d his l78-l81

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L78          16 S L65 FUL
                SAVE TEMP L78 JAI086WPIS/A
                SELECT L78 1- SDCN
L79           7 S E1-E16/DCN OR L78/DCR
L80           3 S L79 AND L32-L38
L81           4 S L79 NOT L80

=> d que l81
L32             QUE  SPE=ON  ABB=ON  PLU=ON  MABIRE, D?/AU
L33             QUE  SPE=ON  ABB=ON  PLU=ON  GUILLEMONT, J?/AU
L34             QUE  SPE=ON  ABB=ON  PLU=ON  VAN DUN, J?/AU
L35             QUE  SPE=ON  ABB=ON  PLU=ON  VANDUN, J?/AU
L36             QUE  SPE=ON  ABB=ON  PLU=ON  SOMERS, M?/AU
L37             QUE  SPE=ON  ABB=ON  PLU=ON  WOUTERS, W?/AU
L38             QUE  SPE=ON  ABB=ON  PLU=ON  JANSSEN/CS,SO,PA
L65             STR
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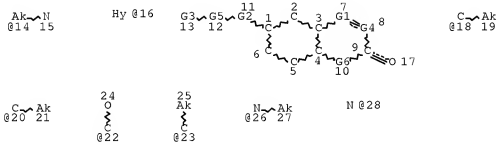


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VAR G1=28/CH/20
REP G2=(0-3) C
VAR G3=N/14/16
VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC    IS R       AT  28
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  27
```

```
CONNECT IS E2  RC AT  28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L78          16 SEA FILE=WPIX SSS FUL L65
L79           7 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (RACQIC/DCN OR RACQID/DCN
                  OR RACQIH/DCN OR RAI9EX/DCN OR RAI9EZ/DCN OR RAI9F0/DCN OR
                 RAJWHA/DCN OR RAMT44/DCN OR RA1G3S/DCN OR RA1G3T/DCN OR
                 RA1G3U/DCN OR RA1G3V/DCN OR RA1G3W/DCN OR RA56SN/DCN OR
                 RA56SP/DCN OR RA56U2/DCN) OR L78/DCR
L80           3 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L79 AND (L32 OR L33 OR
                 L34 OR L35 OR L36 OR L37 OR L38)
L81           4 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L79 NOT L80


=> d his l82

     (FILE 'MEDLINE, BIOSIS, EMBASE, CABA, BIOTECHNO, DRUGU, VETU, AGRICOLA'
     ENTERED AT 10:03:06 ON 08 JAN 2009)
L82           0 S L67

=> d que nos l82
L7                STR
L8  (    1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
                 NC2NC2-C6/ES
L9         22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L65               STR
L67          429 SEA FILE=REGISTRY SUB=L9 SSS FUL L65
L82            0 SEA L67


=> dup rem l72 l81 l82
L82 HAS NO ANSWERS
FILE 'HCAPLUS' ENTERED AT 10:15:37 ON 08 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIX' ENTERED AT 10:15:37 ON 08 JAN 2009
COPYRIGHT (C) 2009 THOMSON REUTERS
PROCESSING COMPLETED FOR L72
PROCESSING COMPLETED FOR L81
PROCESSING COMPLETED FOR L82
L88           42 DUP REM L72 L81 L82 (1 DUPLICATE REMOVED)
                 ANSWERS '1-39' FROM FILE HCAPLUS
                 ANSWERS '40-42' FROM FILE WPIX


=> file stnguide
FILE 'STNGUIDE' ENTERED AT 10:15:52 ON 08 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 6, 2009 (20090106/UP).

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=> d ibib ed abs hitind hitstr 1-20
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX' - CONTINUE? (Y)/N:y



L88  ANSWER 1 OF 42  HCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:469551  HCAPLUS  Full-text
DOCUMENT NUMBER:          144:488409
TITLE:                    N-Acyl anthranilic acid and related compounds as
                          niacin receptor agonists, and their preparation,
                          pharmaceutical compositions and methods of treatment
                          of dyslipidemias
INVENTOR(S):              Colletti, Steven L.; Beresis, Richard T.; Chen,
                          Weichun; Tata, James R.; Shen, Hong C.; Marley, Daria
                          M.; Deng, Qiaolin; Frie, Jessica L.; Ding, Fa-Xiang
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 125 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2006052555        A2    20060518    WO 2005-US39523        20051030
     WO 2006052555        A3    20060622
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     AU 2005305072        A1    20060518    AU 2005-305072         20051030
     CA 2586156           A1    20060518    CA 2005-2586156        20051030
     EP 1809284           A2    20070725    EP 2005-825014         20051030
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
     CN 101056635         A     20071017    CN 2005-80038027       20051030
     JP 2008518957        T     20080605    JP 2007-539301         20051030
     IN 2007CN01653       A     20070831    IN 2007-CN1653         20070423
     US 20070299101       A1    20071227    US 2007-666966         20070502
PRIORITY APPLN. INFO.:                      US 2004-624816P     P  20041104
                                            WO 2005-US39523     W  20051030
OTHER SOURCE(S):          MARPAT 144:488409
ED   Entered STN:  19 May 2006
GI
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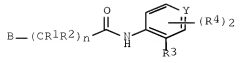

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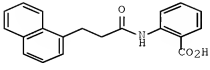

II

AB The invention relates to niacin receptor agonists of formula I; as well as pharmaceutically acceptable salts and solvates. The compds. are useful for treating dyslipidemias, and in particular, reducing serum LDL, VLDL and triglycerides, and raising HDL levels. Pharmaceutical compns. and methods of treatment are also included. Compds. of formula I wherein Y is C or N; R1 and R2 are independently H, (halo)C1-3 alkyl(oxy), OC1-3 alkyl, OH, or F; R3 is Co2H, tetrazolyl, or CONHSO2H and derivs.; R4 is H, halo, or (halo)methyl; B is (un)substituted 10-membered bicyclic aryl, (un)substituted 9- to 10-membered bicyclic heteroaryl, or (un)substituted 12- to 13-membered tricyclic heteroaryl; n is an integer from 1 to 4, such that when (CR1R2)n represent CH(Me)CH2, the ring B is (un)substituted bicyclic aryl; and their pharmaceutically acceptable salts and solvates thereof. Example compound II was prepared by amidation of 3-(1-naphthyl)acrylic acid with Me anthranilate followed by catalytic hydrogenation. All the invention compds. were tested for their niacin receptor affinity. From the assay, it was determined that most of the compds. in general exhibited in vitro EC50 values in the range of about 1 μM to as high as about 100 μM.

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63

IT 571170-77-9P 572874-50-1P 688356-71-0P 688356-91-4P 688356-95-8P
688356-96-9P 688357-06-4P 688357-08-6P 688357-09-7P 688357-10-0P
688357-11-1P 688357-12-2P 688357-13-3P 688357-14-4P 688357-15-5P
688357-16-6P 845829-58-5P 845829-78-9P 854738-63-9P 887342-41-8P
887342-43-0P 887342-45-2P 887342-47-4P 887342-49-6P 887342-51-0P
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887342-91-8P 887342-92-9P 887342-93-0P 887342-94-1P
887342-95-2P 887342-97-4P 887342-98-5P 887342-99-6P 887343-00-2P
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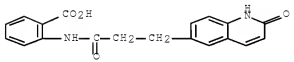
887343-27-3P 887343-29-5P 887343-30-8P 887343-31-9P 887343-32-0P
887343-33-1P 887343-43-3P 887344-07-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-acyl anthranilic acid and related compds.

as niacin receptor agonists and their methods of treatment of dyslipidemias)

IT 887342-92-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-acyl anthranilic acid and related compds. as niacin receptor agonists and their methods of treatment of dyslipidemias)

RN 887342-92-9 HCAPLUS

CN Benzoic acid, 2-[[3-(1,2-dihydro-2-oxo-6-quinolinyl)-1-oxopropyl]amino]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 2 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:501180 HCAPLUS Full-text

DOCUMENT NUMBER: 148:495981

TITLE: Preparation of piperazine-substituted benzothiophenes for treatment of mental disorders

INVENTOR(S): Yamashita, Hiroshi; Matsubara, Jun; Oshima, Kunio; Kuroda, Hideaki; Shimizu, Satoshi; Tanaka, Tatsuyoshi; Taira, Shinichi; Kondo, Kazumi; Takahashi, Haruka; Fukushima, Tae; Sakurai, Yohji

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 312pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

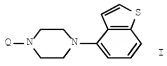
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008047883	A1	20080424	WO 2007-JP70386	20071012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
JP 2008115175	A	20080522	JP 2007-267174	20071012

PRIORITY APPLN. INFO.: JP 2006-280002 A 20061013
JP 2006-280030 A 20061013

OTHER SOURCE(S): MARPAT 148:495981
ED Entered STN: 24 Apr 2008
GI



I

AB An object of the present invention is to provide a heterocyclic compound having a wide therapeutic spectrum, not causing adverse effects and having high safety. The title heterocyclic compds. I [Q = A1N(R12)C(:Z)R11; A1 = alkylene or alkenylene group; Z = O or S; R11 = H, alkyl, aryl, etc.; R12 = H, alkyl, aryl, etc.], useful for treatment and prevention of CNS and mental disorders, were prepared and formulated. Thus, treating N-{4-[4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butyl}ethylamine with acetic anhydride afforded N-{4-[4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butyl}-N-ethylacetamide hydrochloride (II). Exemplified compds. I were tested in dopamine D2 and serotonin 5-HT2A binding assays. For example, II showed Ki of 4.2 nM and 3.0 nM in dopamine D2 and serotonin 5-HT2A binding assays, resp.

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 1021320-11-5P 1021320-12-6P 1021320-13-7P 1021320-14-8P
1021320-15-9P 1021320-16-0P 1021320-17-1P 1021320-18-2P
1021320-19-3P 1021320-20-6P 1021320-21-7P 1021320-22-8P
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1021320-27-3P 1021320-28-4P 1021320-29-5P 1021320-30-8P
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1021320-39-7P 1021320-40-0P 1021320-41-1P 1021320-42-2P
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1021320-48-8P 1021320-49-9P 1021320-50-2P 1021320-51-3P
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1021320-56-8P 1021320-57-9P 1021320-58-0P 1021320-59-1P
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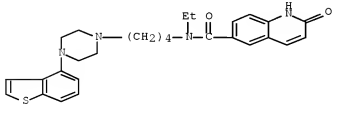
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine-substituted benzothiophenes for treatment and prevention of CNS and mental disorders)

IT 1021320-62-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine-substituted benzothiophenes for treatment and prevention of CNS and mental disorders)

RN 1021320-62-6 HCAPLUS

CN 6-Quinolinecarboxamide, N-[4-(4-benzo[b]thien-4-yl-1-piperazinyl)butyl]-N-ethyl-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 3 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:608275 HCAPLUS Full-text
DOCUMENT NUMBER: 148:561941

TITLE: Piperazine-substituted benzothiophenes and their preparation, pharmaceutical compositions and use in the treatment of mental disorders

INVENTOR(S): Yamashita, Hiroshi; Ito, Nobuaki; Miyamura, Shin; Matsubara, Atsushi; Oshima, Kunio; Kuroda, Hideaki; Shimizu, Satoshi; Takahashi, Hisashi; Tanaka, Tatsuyoshi

PATENT ASSIGNEE(S): Ohtsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 93pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

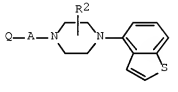
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2008115172	A	20080522	JP 2007-266795	20071012
PRIORITY APPLN. INFO.:			JP 2006-279970 A	20061013

OTHER SOURCE(S): MARPAT 148:561941

ED Entered STN: 22 May 2008

GI



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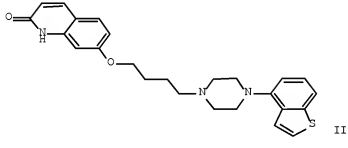

II

AB The invention provides heterocyclic compds. represented by the general formula [I; wherein Q is (un)substituted (hetero)bicyclic ring; R2 is H and lower alkyl; A is O-A1 and lower alkyl; A1 is (un)substituted alkylene] and their salts. The compds. of the invention have a wide treatment spectrum for mental disorders, including central nervous system disorders, with no side effects and high safety and may be useful in the treatment of mental disorders. Example compound (II) was prepared by alkylation of 1-(benzo[b]thien-4-yl)piperazine hydrochloride with 7-(4-chlorobutoxy)-1H-quinolin-2-one. All the invention compds. were evaluated for their dopamine D2 and serotonin 5-HT2A receptor binding affinities. From the assay, it was determined that compound II exhibited Ki values of 0.2 nM and 2.3 nM against D2 and 5-HT2A receptors, resp.

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

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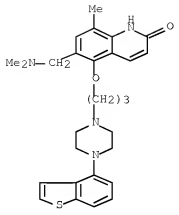
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazine-substituted benzothiophenes useful in treatment and prevention of mental disorders including CNS disorders)

IT 913613-36-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazine-substituted benzothiophenes useful in treatment and prevention of mental disorders including CNS disorders)

RN 913613-36-2 HCAPLUS

CN 2(1H)-Quinolinone, 5-[3-(4-benzo[b]thien-4-yl-1-piperazinyl)propoxy]-6-[(dimethylamino)methyl]-8-methyl- (CA INDEX NAME)



L88 ANSWER 4 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:174406 HCAPLUS Full-text
DOCUMENT NUMBER: 146:251662
TITLE: Xanthine derivatives as selective HM74A agonists and their preparation
INVENTOR(S): Hatley, Richard Jonathan Daniel; Heer, Jag Paul; Liddle, John; Mason, Andrew Mcmurtrie; Pinto, Ivan Leo; Rahman, Shahzad Sharooq; Smith, Ian Edward David
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 312pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007017262	A1	20070215	WO 2006-EP7869	20060808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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IN 2008DN00903	A	20080627	IN 2008-DN903	20080201
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CN 101282976 A 20081008 CN 2006-80037427 20080408
PRIORITY APPLN. INFO.: GB 2005-16464 A 20050810
GB 2006-7736 A 20060419
GB 2006-14569 A 20060721
WO 2006-EP7869 W 20060808
OTHER SOURCE(S): MARPAT 146:251662
ED Entered STN: 16 Feb 2007
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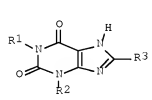

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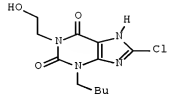

II

AB The invention relates to compds. of formula I, which are xanthine derivs., processes for the manufacture of said derivs., pharmaceutical formulations containing the active compds. and the use of the compds. in therapy, for example, in the treatment of diseases where under-activation of the HM74A receptor contributes to the disease or where activation of the receptor will be beneficial. Compds. of formula I wherein R1 is (un)substituted C1-5 alkylene; R2 is H, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted C2-10 alkynyl, (un)substituted cycloalkyl, (un)substituted cycloalkenyl, (un)substituted heterocyclyl, and (un)substituted (hetero)aryl; R3 is halo and CN; and their pharmaceutically acceptable derivs. thereof, are claimed. Example compound II was prepared by alkylation of 8-chloro-3-pentyl-7-(2-propen-1-yl)-3,7- dihydro-1H-purine-2,6-dione with 2-chloroethanol followed by deallylation. All the invention compds. were evaluated for their HM74A agonistic activity.

CC 26-9 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 28, 45, 63

IT

925246-85-1P	925246-87-3P	925246-89-5P	925246-91-9P	925246-93-1P
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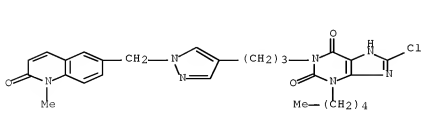
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of xanthine derivs. as selective HM74A agonists)

IT 925248-76-6P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of xanthine derivs. as selective HM74A agonists)

RN 925248-76-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-chloro-1-[3-[1-[(1,2-dihydro-1-methyl-2-oxo-6-quinolinyl)methyl]-1H-pyrazol-4-yl]propyl]-3,9-dihydro-3-pentyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 5 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:174405 HCAPLUS Full-text
DOCUMENT NUMBER: 146:251661

TITLE: Preparation of xanthine derivatives as selective HM74A agonists

INVENTOR(S): Hatley, Richard Jonathan Daniel; Mason, Andrew Mcmurtrie; Pinto, Ivan Leo

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 199pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

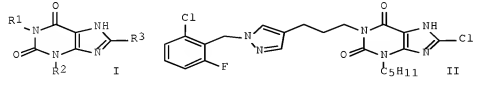
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007017261	A1	20070215	WO 2006-EP7865	20060808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006278215	A1	20070215	AU 2006-278215	20060808
CA 2626723	A1	20070215	CA 2006-2626723	20060808
EP 1912991	A1	20080423	EP 2006-763016	20060808
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
MX 200801931	A	20080324	MX 2008-1931	20080208
IN 2008DN01117	A	20080711	IN 2008-DN1117	20080208
KR 2008034993	A	20080422	KR 2008-705717	20080307
NO 2008001211	A	20080508	NO 2008-1211	20080307
CN 101282977	A	20081008	CN 2006-80037470	20080408

PRIORITY APPLN. INFO.:			
	GB 2005-16464	A	20050810
	GB 2006-7736	A	20060419
	GB 2006-14569	A	20060721
	WO 2006-EP7865	W	20060808

OTHER SOURCE(S): MARPAT 146:251661

ED Entered STN: 16 Feb 2007

GI



AB Xanthine derivs. of formula I [R1 = (CH2)mX(CH2)nY; X = heteroaryl, heterocyclyl; Y = (substituted) aryl, heteroaryl, aryloxy; m = 3-4; n = 0-1; R2 = (substituted) alkyl; R3 = halo] are prepared for the treatment of diseases where under-activation of the HM74A receptor contributes to the

disease or where activation of the receptor will be beneficial. Thus, II was prepared from 3-pentyl-8-chloro-7-allyl-3,7-dihydro-1H-purine-2,6-dione, 4-(3-hydroxypropyl)pyrazole and 2-chloro-6-fluorobenzyl bromide. The prepared compds. had pEC50 values ≥ 4.3 and efficacy ≥ 30% in GTPγS binding assays.

CC 26-9 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

IT

925246-85-1P	925246-87-3P	925246-89-5P	925246-91-9P	925246-93-1P
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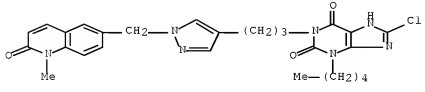
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthine derivs. as selective HM74A agonists)

IT 925248-76-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of xanthine derivs. as selective HM74A agonists)
RN 925248-76-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-chloro-1-[3-[1-[(1,2-dihydro-1-methyl-2-oxo-6-quinolinyl)methyl]-1H-pyrazol-4-yl]propyl]-3,9-dihydro-3-pentyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 6 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1452342 HCAPLUS Full-text
DOCUMENT NUMBER: 148:158850
TITLE: Comparative Molecular Field Analysis of quinoline derivatives as selective and noncompetitive mGluR1 antagonists
AUTHOR(S): Sekhar, Y. Nataraja; Nayana, M. Ravi Shashi; Ravikumar, Muttineni; Mahmood, S. k.
CORPORATE SOURCE: Bioinformatics Division, Department of Environmental Microbiology, Osmania University, Hyderabad, India
SOURCE: Chemical Biology & Drug Design (2007), 70(6), 511-519 CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Dec 2007
AB A 3D-QSAR Comparative Mol. Field Anal. (Co-MFA) of 45 quinoline derivs. as metabotropic glutamate receptor subtype 1 (mGluR1) inhibitors was investigated. The Co-MFA anal. provided a model with q2 value of 0.827 and r2 value of 0.990, in which q2 value of 0.827 and an r2 value of 0.990, in which the good correlation between the inhibitory activities and the steric and electrostatic mol. field around the analogs was observed The predictive ability of the models was validated using the set of 12 compds. that were not included in the training set of 33 compds. These results provided further understanding of the relationship between the structural features of quinolone derivs. and its activities, which should be applicable to design and find new potential mGluR1 inhibitors.
CC 1-3 (Pharmacology)
IT 409340-64-3 409340-65-4 409340-66-5 409340-67-6 409340-86-9
409340-94-9 409341-55-5 409341-57-7 409341-58-8 409341-59-9
409341-60-2 409341-61-3 409341-85-1 409341-93-1 409341-99-7
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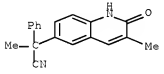
1003022-62-5 1003022-63-6 1003022-65-8 1003022-66-9 1003022-67-0
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)
(comparative mol. field anal. of quinoline derivs. as selective and noncompetitive mGluR1 antagonists)

IT 854533-56-5
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative mol. field anal. of quinoline derivs. as selective and noncompetitive mGluR1 antagonists)

RN 854533-56-5 HCAPLUS

CN 6-Quinolineacetonitrile, 1,2-dihydro-α,3-dimethyl-2-oxo-α-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 7 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1120580 HCAPLUS Full-text
DOCUMENT NUMBER: 145:471562
TITLE: Piperazine-substituted benzothiophenes and their preparation, pharmaceutical compositions and use in the treatment of mental disorders
INVENTOR(S): Yamashita, Hiroshi; Matsubara, Jun; Oshima, Kunio; Kuroda, Hideaki; Ito, Nobuaki; Miyamura, Shin; Shimizu, Satoshi; Tanaka, Tatsuyoshi; Oshiro, Yasuo; Shimada, Jun; Maeda, Kenji; Tadori, Yoshihiro; Amada, Naoki; Akazawa, Hitomi; Yamashita, Junko; Mori, Atsushi; Uwahodo, Yasufumi; Masumoto, Takumi; Kikuchi, Tetsuro; Hashimoto, Kazuya; Takahashi, Haruka
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 178pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006112464	A1	20061026	WO 2006-JP308162	20060412

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006237905	A1	20061026	AU 2006-237905		20060412
CA 2602247	A1	20061026	CA 2006-2602247		20060412
EP 1869025	A1	20071226	EP 2006-732069		20060412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR					
JP 2006316052	A	20061124	JP 2006-111241		20060413
IN 2007DN07041	A	20071005	IN 2007-DN7041		20070912
KR 2008002817	A	20080104	KR 2007-723158		20071010
MX 200712626	A	20080111	MX 2007-12626		20071011
CN 101155804	A	20080402	CN 2006-80011923		20071012
PRIORITY APPLN. INFO.:			JP 2005-116698	A	20050414
			WO 2006-JP308162	W	20060412
			WO 2006-JP8162	W	20060412

OTHER SOURCE(S): MARPAT 145:471562

ED Entered STN: 26 Oct 2006

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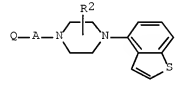

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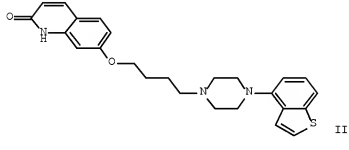

II

AB The invention provides a heterocyclic compound represented by the general formula I: The compds. of the invention have a wide treatment spectrum for mental disorders, including central nervous system disorders, with no side effects and high safety. Compds. of formula I wherein Q is (un)substituted (hetero)bicyclic ring; R2 is H and lower alkyl; A is O-A1 and lower alkyl; A1 is (un)substituted alkylene; and their salts are claimed. Example compound II was prepared by alkylation of 1-(benzo[b]thien-4-yl)piperazine hydrochloride with 7-(4-chlorobutoxy)-1H-quinolin-2-one. All the invention compds. were evaluated for their dopamine D2 and serotonin 5-HT2A receptor binding affinities. From the assay, it was determined that compound II exhibited Ki values of 0.2 nM and 2.3 nM against D2 and 5-HT2A receptors, resp. These compds. may be useful in the treatment of mental disorders.

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 913611-98-0P 913611-99-1P 913612-00-7P 913612-01-8P 913612-02-9P
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913613-75-9P 913613-76-0P 913613-77-1P 913613-79-3P 913613-80-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine-substituted benzothiophenes useful in treatment and prevention of mental disorders including CNS disorders)

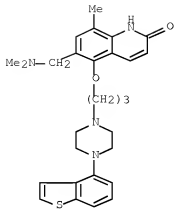
IT 913613-36-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine-substituted benzothiophenes useful in treatment and prevention of mental disorders including CNS disorders)

RN 913613-36-2 HCAPLUS

CN 2(1H)-Quinolinone, 5-[3-(4-benzo[b]thien-4-yl-1-piperazinyl)propoxy]-6-[(dimethylamino)methyl]-8-methyl- (CA INDEX NAME)

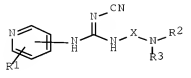


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 8 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:632795 HCAPLUS Full-text
DOCUMENT NUMBER: 145:103569
TITLE: Preparation of novel pyridyl cyanoguanidine compounds for treating hyperproliferative and neoplastic diseases
INVENTOR(S): Bjoerkling, Fredrik; Dannacher, Heinz Wilhelm
PATENT ASSIGNEE(S): Leo Pharma A/S, Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006066584	A1	20060629	WO 2005-DK803	20051220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2594508	A1	20060629	CA 2005-2594508	20051220
EP 1838696	A1	20071003	EP 2005-820855	20051220
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008524269	T	20080710	JP 2007-547180	20051220
US 20080312275	A1	20081218	US 2008-793867	20080523
PRIORITY APPLN. INFO.:			US 2004-637757P	P 20041222
			WO 2005-DK803	W 20051220

OTHER SOURCE(S): CASREACT 145:103569; MARPAT 145:103569
ED Entered STN: 30 Jun 2006
GI



I

AB The title compds. I [X = (un)substituted (un)saturated alkyl diradical; R1 = H, halo, alkyl, etc.; NR2R3 = (un)substituted 5-12 membered mono-or bicyclic ring system optionally including one or more addnl. heteroatoms selected from N, S or O, said ring system being substituted with a group :O at one carbon atom thereof] which exhibit a high antiproliferative activity and may be used in the treatment of hyperproliferative and neoplastic diseases, were prepared Thus, reacting 1-(6-amino-1-hexyl)-1,2-dihydroquinolin-2-one (preparation given) with S-methyl-N-cyano-N'-4-pyridyl-isothiourea in the presence of Et3N and DMAP and pyridine afforded N-[6-(2-oxo-1,2-dihydro-1-quinolinyl)-1-hexyl]-N'- cyano-N''-(4-pyridyl)guanidine. It has been found that compds. I are capable of modulation the activity of IκB kinase (no specific data given). Pharmaceutical compns. comprising the compound I alone or in combination with other therapeutic agents are disclosed.

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

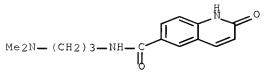
IT 39497-01-3P 896133-86-1P 896133-87-2P 896133-88-3P 896133-89-4P
896133-90-7P 896133-91-8P 896133-92-9P 896133-93-0P 896133-94-1P
896133-95-2P 896133-96-3P 896133-97-4P 896133-98-5P
896133-99-6P 896134-00-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel pyridyl cyanoguanidine compds. with high antiproliferative activity useful for treating hyperproliferative and neoplastic diseases)

IT 896133-97-4P 896133-99-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel pyridyl cyanoguanidine compds. with high antiproliferative activity useful for treating hyperproliferative and neoplastic diseases)

RN 896133-97-4 HCAPLUS

CN 6-Quinolinecarboxamide, 1,2-dihydro-N-(2-hydroxyethyl)-2-oxo- (CA INDEX NAME)

RN 896133-99-6 HCAPLUS
CN 6-Quinolinecarboxamide, N-[3-(dimethylamino)propyl]-1,2-dihydro-2-oxo-
(CA INDEX NAME)



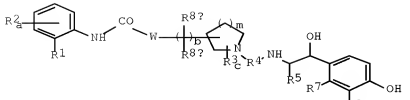
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 9 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:148698 HCAPLUS Full-text
DOCUMENT NUMBER: 144:232927
TITLE: Preparation of piperidine and related derivatives having β2 adrenergic receptor agonist and muscarinic receptor antagonist activity
INVENTOR(S): Mammen, Mathai; Mischki, Trevor; Hughes, Adam; Ji, Yu-Hua
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

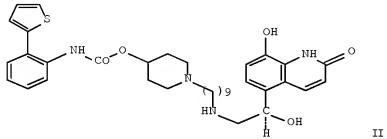
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060035933	A1	20060216	US 2005-204263	20050815
WO 2006023460	A2	20060302	WO 2005-US29024	20050815
WO 2006023460	A3	20060406		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1833822	A2	20070919	EP 2005-785501	20050815
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
JP 2008510015	T	20080403	JP 2007-527922	20050815

PRIORITY APPLN. INFO.: US 2004-601779P P 20040816
WO 2005-US29024 W 20050815

OTHER SOURCE(S): MARPAT 144:232927
ED Entered STN: 17 Feb 2006
GI



I



II

AB This invention provides compds. (shown as I; variables defined below; e.g. [2-(thien-2-yl)phenyl]carbamic acid 1-[9-[[(R)-2-hydroxy-2-(8-hydroxy-2-oxo-1,2-dihydroquinolin-5- yl)ethyl]amino]nonyl]piperidin-4-yl ester (shown as II)) or a pharmaceutically acceptable salt or solvate or stereoisomer thereof. The compds. possess both β2 adrenergic receptor agonist and muscarinic receptor antagonist activity. Accordingly, such compds. are expected to be useful as therapeutic agents for treating pulmonary disorders, such as chronic obstructive pulmonary disease and asthma. Methods of preparation are claimed and prepns. and/or characterization data for 14 examples of I are included. For example, II was prepared in 2 steps from [2-(thien-2-yl)phenyl]carbamic acid 1-[8-([1,3]dioxolan-2-yl)octyl]piperidin-4-yl ester (preparation given) by 1st deprotecting it and combining the intermediate under reducing conditions with 5-[(R)-2-amino-1-[(tert-butyldimethylsilanyl)oxy]ethyl]-8-hydroxy-1H- quinolin-2-one acetate (preparation given). For I: W = O or NWa; where Wa is H or (1-4C)alkyl; R1 is (un)substituted (2-9C)heteroaryl containing = 1-4 heteroatoms = O, N and S or (3-7C)cycloalkyl; each R2 = (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, -OR2a, -C(O)OR2b, -SR2c, -S(O)R2d, -S(O)2R2e and -NR2fR2g; where each of R2a, R2b, R2c, R2d, R2e, R2f and R2g = H, (1-4C)alkyl or phenyl(1-4C)alkyl; and where each alkyl group present in R2 is (un)substituted with 1-3 fluoro substituents. Each R3 = (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, -OR3a, -C(O)OR3b, -SR3c, -S(O)R3d, -S(O)2R3e and -NR3fR3g; or two R3 groups are joined to form (1-3C)alkylene, (2-3C)alkenylene or oxiran-2,3-diyl; where each of R3a, R3b, R3c, R3d, R3e, R3f and R3g = H, (1-4C)alkyl or phenyl(1-4C)alkyl; R4 = a divalent hydrocarbon group containing = 4-28 C atoms and optionally containing = 1-10 heteroatoms = halo, O, N and S, provided that the number of contiguous atoms in the shortest chain between the two N atoms to which R4 is attached = 4-16. R5 = H or (1-4C)alkyl; R6 is -N(R6a)C(O)R6b or -CR6cR6dOR6e and R7 is H; or R6 and R7 together form -N(R7a)C(O)C(R7b):C(R7c)-, -C(R7d):C(R7c)C(O)N(R7f)-, -N(R7g)C(O)CR7hR7i-CR7jR7k- or -CR7lR7m-CR7nR7oC(O)-N(R7p)-; where each of R6a, R6b, R6c, R6d and R6e = H and (1-4C)alkyl; and each of R7a, R7b, R7c, R7d, R7e, R7f, R7g, R7h, R7i, R7j, R7k, R7l, R7m, R7n, Ro and R7p = H and (1-4C)alkyl; each R8a and R8b

= H, (1-4C)alkyl, hydroxy and fluoro, or R8a and R8b together with the atoms to which they are attached form a (3-6C)cycloalkyl ring or a (2-5C)heterocyclic ring containing 1 or 2 heteroatoms = O, N and S; a = 0-3; b = 0-5; c = 0-4; m = 0-3; addnl. details are given in the claims. A method of studying a biol. system or sample comprising a muscarinic receptor or a β2 adrenergic receptor using I is also claimed.

INCL 514316000; 514326000; 546186000; 546206000; 546208000; 546193000; 514318000; 514319000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

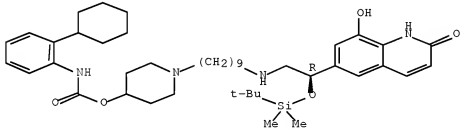
IT 20896-27-9 54030-34-1 84913-19-9 102293-80-1 452342-05-1
743460-69-7 743461-60-1 1022158-39-9 1057248-83-5 1057248-84-6
1057248-85-7 1057248-86-8 1057248-87-9 1057248-88-0
1057248-89-1 1057248-90-4 1057248-91-5 1057248-92-6
1057248-93-7 1057248-94-8 1057248-95-9 1057248-96-0 1057248-97-1
1057248-98-2
RL: PRPH (Prophetic)
(Preparation of piperidine and related derivatives having β2 adrenergic receptor agonist and muscarinic receptor antagonist activity)

IT 1057248-89-1
RL: PRPH (Prophetic)
(Preparation of piperidine and related derivatives having β2 adrenergic receptor agonist and muscarinic receptor antagonist activity)

RN 1057248-89-1 HCAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L88 ANSWER 10 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:962196 HCAPLUS Full-text

DOCUMENT NUMBER: 143:266597

TITLE: Preparation of benzamides and nitrogen-heterocycle carboxamides as NMDA NR2B receptor antagonists with therapeutic uses

INVENTOR(S): Kawai, Makoto; Kawamura, Mitsuhiro; Sakurada, Isao; Morita, Asato

PATENT ASSIGNEE(S): Pfizer Japan, Inc., Japan; Pfizer Inc.

SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

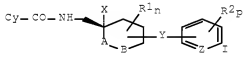
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005080317	A2	20050901	WO 2005-IB258	20050201
WO 2005080317	A3	20060216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2555970	A1	20050901	CA 2005-2555970	20050201
EP 1716100	A2	20061102	EP 2005-702407	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
BR 2005007636	A	20070710	BR 2005-7636	20050201
US 20070167452	A1	20070719	US 2006-597868	20060810
MX 2006PA09198	A	20061003	MX 2006-PA9198	20060811
PRIORITY APPLN. INFO.:			US 2004-544258P P	20040211
			WO 2005-IB258 W	20050201

OTHER SOURCE(S): CASREACT 143:266597; MARPAT 143:266597
ED Entered STN: 02 Sep 2005
GI



AB The present invention relates to benzamides and nitrogen-heterocycle carboxamides (shown as I; variables defined below; e.g. 4-hydroxy-N-[[cis-4-(phenoxymethyl)cyclohexyl]methyl]benzamide) or a pharmaceutically acceptable salt or solvate thereof, to processes for the preparation of, intermediates used in the preparation of, compns. containing such compds. and the uses of such compds. as antagonists of the NMDA NR2B receptor. For I: A and B = CH2 or O, with the proviso that A and B are not simultaneously O; Cy = one of 30 ring radicals, e.g. 4-hydroxyphenyl and 1H-pyrazol-4-yl (un)substituted by 1-3 hydroxy, halogen, C1-6alkyl, C1-6alkoxy, C1-6 haloalkyl, C1-6alkylamino and amino; R1 and R2 = hydroxy, halogen, C1-6alkyl, C1-6alkoxy, C1-6 haloalkyl and C3-8 cycloalkyl; n = 0-4; X is H, hydroxy, halogen or C1-6alkoxy; Y is oxy, thio, a 1-4 membered alkylene, a 2-4 membered alkylene ether, 2-4 membered alkylene thioether or an oxyethyleneoxy group, (un)substituted by 1-4 hydroxy, halogen, C1-6alkyl, C1-6alkoxy and C1-6 haloalkyl; Z is CH or N; and p = 0-5 when Z is CH or 0-4 when Z is N; when p = ≥2, two of R2s may be taken together with the C atoms to which they are attached to form a 5-8 membered cycloalkyl ring. Although the methods of preparation are not claimed, >130 example prepns. for I and >180 for intermediates are included. For example, II was prepared by condensation of 4-(benzyloxy)-N-[[cis-4-(hydroxymethyl)cyclohexyl]methyl]benzamide with phenol using DIAD and PPh3

followed by debenzylation via hydrogenation over 10 % Pd-C. Results for some I in NR2B and human dofetilide binding assays are tabulated.

IC ICM C07C235-00

CC 23-18 (Aliphatic Compounds)
Section cross-reference(s): 1, 63

IT 863563-15-9P, 4-Hydroxy-N-[[cis-4-(phenoxymethyl)cyclohexyl]methyl]benzamide sodium salt 863563-16-0P, 4-Hydroxy-N-[[cis-4-[(4-methoxyphenoxy)methyl]cyclohexyl]methyl]benzamide 863563-18-2P, N-[[cis-4-(Benzyloxy)cyclohexyl]methyl]-4-hydroxybenzamide 863563-20-6P, N-[[cis-4-[(4-Chlorobenzyl)oxy]cyclohexyl]methyl]-4-hydroxybenzamide 863563-22-8P, N-[[cis-4-[(3-Chlorobenzyl)oxy]cyclohexyl]methyl]-4-hydroxybenzamide 863563-23-9P, 4-Hydroxy-N-[[cis-4-(4-methoxyphenoxy)cyclohexyl]methyl]benzamide 863563-25-1P, N-[[cis-4-(4-Chlorophenoxy)cyclohexyl]methyl]-4-hydroxybenzamide 863563-27-3P, 4-Hydroxy-N-[[trans-1-hydroxy-4-(phenoxymethyl)cyclohexyl]methyl]benzamide 863563-29-5P, N-[[trans-4-[(4-Fluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-31-9P, N-[[trans-4-[(3-Fluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-32-0P, N-[[trans-4-[(2-Fluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-33-1P, N-[[trans-4-[(2,6-Difluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-34-2P, N-[[trans-4-[(3,5-Difluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-35-3P, N-[[trans-4-[(2-Chlorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-36-4P, N-[[trans-4-[(3-Chlorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-37-5P, N-[[trans-4-[(4-Chlorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-38-6P, 4-Hydroxy-N-[[trans-1-hydroxy-4-[[(2-methylphenyl)oxy]methyl]cyclohexyl]methyl]benzamide 863563-39-7P, 4-Hydroxy-N-[[trans-1-hydroxy-4-[[(3-methylphenyl)oxy]methyl]cyclohexyl]methyl]benzamide 863563-40-0P, 4-Hydroxy-N-[[trans-1-hydroxy-4-[[(4-methylphenyl)oxy]methyl]cyclohexyl]methyl]benzamide 863563-41-1P, 4-Hydroxy-N-[[trans-1-hydroxy-4-[(3-methoxyphenoxy)methyl]cyclohexyl]methyl]benzamide 863563-42-2P, N-[[trans-4-[(Benzyloxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-45-5P, N-[[trans-4-[[(2-Fluorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide sodium salt 863563-46-6P, N-[[trans-4-[[(3-Fluorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-47-7P, N-[[trans-4-[[(4-Fluorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-48-8P, N-[[trans-4-[[(4-Chlorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-49-9P, 4-Hydroxy-N-[[trans-1-hydroxy-4-(2-phenoxyethyl)cyclohexyl]methyl]benzamide 863563-51-3P, N-[[trans-4-[2-(2-Fluorophenoxy)ethyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-52-4P, N-[[trans-4-[2-(3-Fluorophenoxy)ethyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-53-5P, N-[[trans-4-[2-(4-Fluorophenoxy)ethyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-54-6P, N-[[trans-4-(Benzyloxy)-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-56-8P, N-[[trans-4-(4-Chlorophenoxy)-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-57-9P, N-[[cis-4-(4-Chlorophenoxy)-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-59-1P, N-[[trans-4-(4-Chlorophenoxy)-1-hydroxycyclohexyl]methyl]-3-fluoro-4-hydroxybenzamide 863563-60-4P, N-[[cis-4-(4-Chlorophenoxy)-1-hydroxycyclohexyl]methyl]-3-fluoro-4-hydroxybenzamide 863563-61-5P, (+)-4-Hydroxy-N-[[(2S,5S)-5-(phenoxymethyl)tetrahydro-2H-pyran-2-yl]methyl]benzamide 863563-62-6P, (-)-4-Hydroxy-N-[[(2R,5R)-5-(phenoxymethyl)tetrahydro-2H-pyran-2-

yl]methyl]benzamide 863563-63-7P,
4-Hydroxy-N-[[(2S,5R)-5-(phenoxymethyl)tetrahydro-2H-pyran-2-yl]methyl]benzamide 863563-64-8P,
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4-Hydroxy-N-[[(2R,5S)-5-[(benzyloxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]benzamide 863563-71-7P,
(-)-4-Hydroxy-N-[[(3R,6S)-6-(phenoxymethyl)tetrahydro-2H-pyran-3-yl]methyl]benzamide 863563-72-8P,
(+)-4-Hydroxy-N-[[(3S,6R)-6-(phenoxymethyl)tetrahydro-2H-pyran-3-yl]methyl]benzamide 863563-73-9P,
(+)-4-Hydroxy-N-[[(3R,6R)-6-(phenoxymethyl)tetrahydro-2H-pyran-3-yl]methyl]benzamide 863563-75-1P,
(-)-4-Hydroxy-N-[[(3S,6S)-6-(phenoxymethyl)tetrahydro-2H-pyran-3-yl]methyl]benzamide 863563-78-4P,
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3-Fluoro-N-[[trans-4-[(3-fluorobenzyl)oxy]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-84-2P, 3-Fluoro-N-[[trans-4-[[(3-fluorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-86-4P, 3-Fluoro-N-[[trans-4-[2-(2-fluorophenoxy)ethyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863563-89-7P,
N-[[cis-4-(4-Chlorophenoxy)cyclohexyl]methyl]-3-fluoro-4-hydroxybenzamide 863563-90-0P, N-[[trans-4-(4-Chlorophenoxy)cyclohexyl]methyl]-3-fluoro-4-hydroxybenzamide 863563-92-2P, 3-Fluoro-4-hydroxy-N-[(4-phenoxycyclohexyl)methyl]benzamide 863563-94-4P,
N-[[cis-4-(4-Fluorophenoxy)cyclohexyl]methyl]-4-hydroxybenzamide 863563-96-6P, 3-Fluoro-N-[[cis-4-(4-fluorophenoxy)cyclohexyl]methyl]-4-hydroxybenzamide 863563-99-9P, N-[[trans-4-[2-(2-Fluorophenoxy)ethyl]-1-hydroxycyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-01-6P,
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N-[[trans-4-[(Benzyloxy)methyl]-1-hydroxycyclohexyl]methyl]-3-fluoro-4-hydroxybenzamide 863564-13-0P, N-[[cis-4-[(Benzyloxy)methyl]cyclohexyl]methyl]-4-hydroxybenzamide 863564-16-3P,
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3-Fluoro-N-[[trans-4-[(2-fluorophenoxy)methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863564-26-5P,
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4-Hydroxy-N-[[trans-1-hydroxy-4-[[(5-methylpyridin-2-yl)oxy]methyl]cyclohexyl]methyl]benzamide 863564-30-1P,
N-[(trans-4-Benzyl-1-hydroxycyclohexyl)methyl]-4-hydroxybenzamide 863564-32-3P, 3-Fluoro-N-[[trans-4-[[(2-fluorobenzyl)oxy]methyl]-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863564-34-5P,

4-Hydroxy-N-[[trans-4-(phenoxymethyl)cyclohexyl]methyl]benzamide
863564-36-7P, 6-Hydroxy-N-[[cis-4-(2-phenylethoxy)cyclohexyl]methyl]nicotinamide 863564-37-8P, N-[[cis-4-(2-Phenylethoxy)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-38-9P, N-[[cis-4-(Phenoxymethyl)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-40-3P, N-[[(3R,6S)-6-[(4-Fluorophenoxy)methyl]tetrahydro-2H-pyran-3-yl]methyl]-4-hydroxybenzamide 863564-46-9P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-48-1P, 4-Hydroxy-N-[[cis-4-(2-phenoxyethoxy)cyclohexyl]methyl]benzamide 863564-50-5P, 2-Oxo-N-[[cis-4-(2-phenylethoxy)cyclohexyl]methyl]-2,3-dihydro-1,3-benzoxazole-6-carboxamide 863564-52-7P, 3-Fluoro-N-[[trans-4-(4-fluorobenzyl)-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863564-54-9P, N-[[trans-4-(4-Fluorobenzyl)-1-hydroxycyclohexyl]methyl]-4-hydroxybenzamide 863564-55-0P, 6-Hydroxy-N-[[cis-4-(phenoxymethyl)cyclohexyl]methyl]nicotinamide 863564-56-1P, 2-Hydroxy-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]isonicotinamide 863564-57-2P, 6-Hydroxy-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]nicotinamide 863564-58-3P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-pyrazole-3-carboxamide 863564-59-4P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-imidazole-4-carboxamide 863564-60-7P, 5-Chloro-6-hydroxy-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]nicotinamide 863564-61-8P, 3-Fluoro-N-[[cis-4-[[(5-fluoropyridin-2-yl)oxy]methyl]cyclohexyl]methyl]-4-hydroxybenzamide 863564-63-0P, 3-Fluoro-4-hydroxy-N-[[cis-4-[(pyridin-2-yloxy)methyl]cyclohexyl]methyl]benzamide 863564-65-2P, N-[[cis-4-[2-(4-Fluorophenoxy)ethoxy]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-67-4P, 3,5-Difluoro-4-hydroxy-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]benzamide 863564-68-5P, 6-Oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-1,4,5,6-tetrahydropyridazine-3-carboxamide 863564-69-6P, 6-Oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-1,6-dihydropyridazine-3-carboxamide 863564-70-9P, N-[[cis-4-[2-(2-Fluorophenoxy)ethyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-72-1P, N-[[cis-4-[2-(4-Fluorophenoxy)ethoxy]cyclohexyl]methyl]-6-hydroxynicotinamide 863564-73-2P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-pyrrole-3-carboxamide 863564-74-3P, 2-Oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]indoline-5-carboxamide 863564-75-4P, 2-Oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-1,2,3,4-tetrahydroquinoline-6-carboxamide 863564-76-5P, 3-Methyl-2-oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-2,3-dihydro-1H-benzimidazole-5-carboxamide 863564-78-7P, N-[[cis-4-[(2-Fluorophenoxy)methyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-80-1P, 2-Oxo-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-2,3-dihydro-1,3-benzothiazole-6-carboxamide 863564-81-2P, 3-Amino-N-[[cis-4-(2-phenoxyethyl)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-82-3P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-indazole-5-carboxamide 863564-83-4P, N-[[cis-4-(2-Phenoxyethyl)cyclohexyl]methyl]-1H-1,2,3-triazole-4-carboxamide 863564-84-5P, N-[[cis-4-[(Pyridin-2-yloxy)methyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-85-6P, N-[[cis-4-[(3-Fluorophenoxy)methyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-87-8P, N-[[cis-4-(3-Phenoxypropyl)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-89-0P, 3,5-Difluoro-4-hydroxy-N-[[cis-4-(phenoxymethyl)cyclohexyl]methyl]benzamide 863564-90-3P, N-[[cis-4-[(4-Fluorophenoxy)methyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-92-5P, N-[[cis-4-(Benzyloxy)cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-93-6P,

N-[[cis-4-[(3-Methoxyphenoxy)methyl]cyclohexyl]methyl]-1H-pyrazole-4-carboxamide 863564-95-8P 863564-97-0P,
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N-[[(2R,5R)-5-[(4-Chlorophenoxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]-2-oxo-1,2,3,4-tetrahydroquinoline-6-carboxamide 863565-21-3P,
N-[[(2R,5R)-5-[(4-Chlorophenoxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]-3-methyl-1H-pyrazole-4-carboxamide 863565-22-4P,
N-[[(2R,5R)-5-[(4-Chloro-3-fluorophenoxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863565-23-5P,
3-Amino-N-[[(2R,5R)-5-[[(4-ethylphenyl)oxy]methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863565-24-6P 863565-25-7P,
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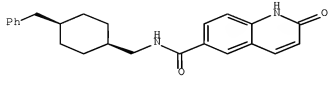
3-Amino-N-[[(2R,5R)-5-[(3-fluoro-4-methylphenoxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863565-28-0P,
N-[[(2R,5R)-5-[(3-Fluoro-4-methylphenoxy)methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863565-29-1P,
3-Amino-N-[[(2R,5R)-5-[[(2,3-dihydro-1H-inden-5-yl)oxy]methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863565-30-4P,
N-[[(2R,5R)-5-[[(2,3-Dihydro-1H-inden-5-yl)oxy]methyl]tetrahydro-2H-pyran-2-yl]methyl]-1H-pyrazole-4-carboxamide 863566-63-6P,
4-Hydroxy-N-[[1-hydroxy-4-(phenoxymethyl)cyclohexyl]methyl]benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzamides and nitrogen-heterocycle carboxamides as NMDA NR2B receptor antagonists with therapeutic uses)

IT 863565-14-4P, N-[(cis-4-Benzylcyclohexyl)methyl]-2-hydroxyquinoline-6-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzamides and nitrogen-heterocycle carboxamides as NMDA NR2B receptor antagonists with therapeutic uses)

RN 863565-14-4 HCAPLUS

CN 6-Quinolinecarboxamide, 1,2-dihydro-2-oxo-N-[[cis-4-(phenylmethyl)cyclohexyl]methyl]- (CA INDEX NAME)

Relative stereochemistry.



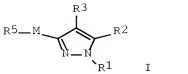
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 11 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:182700 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235705
TITLE: Preparation of pyrazole derivatives as antagonists of gonadotropin releasing hormone (gnrh) for treating sex hormone related conditions
INVENTOR(S): Bird, Thomas Geoffrey Colerick; Herdemann, Matthias Ferdinand; Maudet, Mickael Louis Pierre
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017961	A2	20040304	WO 2003-GB3633	20030819
WO 2004017961	A3	20040408		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003255820	A1	20040311	AU 2003-255820	20030819
EP 1531811	A2	20050525	EP 2003-792487	20030819
EP 1531811	B1	20081029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006505528	T	20060216	JP 2004-530361	20030819
AT 412412	T	20081115	AT 2003-792487	20030819
US 20060287379	A1	20061221	US 2005-524977	20051128

PRIORITY APPLN. INFO.: EP 2002-292077 A 20020821
WO 2003-GB3633 W 20030819

OTHER SOURCE(S): MARPAT 140:235705
ED Entered STN: 05 Mar 2004
GI



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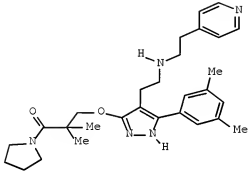

II

AB Title compds. I [R1 = H, (un)substituted-alkyl, aryl, or arylalkyl; R2 = (un)substituted mono or bicyclic aromatic ring; R3 = arylalkylaminoalkyl, heterocyclylalkylaminoalkyl, etc.; M = -(CH2)0-2O-, or -CONH-; R5 = H, halo, heterocyclylcarbonylalkyl, etc.] and their pharmaceutically acceptable salts are prepared and disclosed as gonadotropin releasing hormone antagonists. Thus, e.g., II, was prepared in a multistep synthesis from Me 3,5-dimethylbenzoate and butyrolactone. In test assays, I possessed activity at concns. from 1 nM to 5 μM.

IC ICM A61K031-4155

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 2, 63

IT 667459-73-6P 667459-74-7P 667459-75-8P 667459-76-9P 667459-77-0P
667459-78-1P 667459-79-2P 667459-80-5P 667459-81-6P 667459-82-7P
667459-83-8P 667459-84-9P 667459-85-0P 667459-86-1P 667459-87-2P
667459-88-3P 667459-89-4P 667459-90-7P 667459-91-8P 667459-92-9P
667459-93-0P 667459-94-1P 667459-95-2P 667459-96-3P 667459-97-4P
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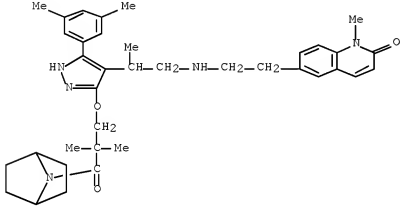
667460-66-4P 667460-67-5P 667460-68-6P 667460-69-7P 667460-70-0P
667460-71-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazoles as antagonists of gonadotropin releasing hormone)

IT 667460-37-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazoles as antagonists of gonadotropin releasing hormone)

RN 667460-37-9 HCAPLUS

CN 2(1H)-Quinolinone, 6-[2-[[(2S)-2-[3-[3-(7-azabicyclo[2.2.1]hept-7-yl)-2,2-dimethyl-3-oxopropoxy]-5-(3,5-dimethylphenyl)-1H-pyrazol-4-yl]propyl]amino]ethyl]-1-methyl- (CA INDEX NAME)



L88 ANSWER 12 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

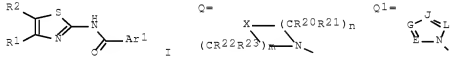
ACCESSION NUMBER: 2003:591177 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149652
TITLE: Preparation of 2-acylaminothiazole derivatives or salts thereof as c-Mpl receptor ligands
INVENTOR(S): Sugasawa, Keizo; Watanuki, Susumu; Koga, Yuji; Nagata, Hiroshi; Obitsu, Kazuyoshi; Wakayama, Ryutaro; Hirayama, Fukushi; Suzuki, Ken-ichi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062233	A1	20030731	WO 2003-JP270	20030115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,				

UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2472711	A1	20030731	CA 2003-2472711		20030115
EP 1466912	A1	20041013	EP 2003-700571		20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1639157	A	20050713	CN 2003-804457		20030115
CN 1319967	C	20070606			
JP 4120586	B2	20080716	JP 2003-562111		20030115
IN 2004KN00942	A	20060217	IN 2004-KN942		20040705
US 20050153977	A1	20050714	US 2004-500964		20040708
JP 2008111001	A	20080515	JP 2008-23950		20080204
PRIORITY APPLN. INFO.:			JP 2002-10413	A	20020118
			JP 2002-10447	A	20020118
			JP 2003-562111	A3	20030115
			WO 2003-JP270	W	20030115

OTHER SOURCE(S): MARPAT 139:149652
ED Entered STN: 01 Aug 2003
GI



AB 2-Acylaminothiazole derivs. or pharmaceutically acceptable salts thereof [I; Ar1 = each (un)substituted aryl, monocyclic aromatic heterocyclyl, or bicyclic condensed heterocyclyl; R1 = each (un)substituted aryl or monocyclic aromatic heterocyclyl; R2 = Q, Q1, R24R25N; wherein n, m = an integer of 1-3; when n or m is an integer of ≥2, CR20R21 and CR22R23 may represent a different group; X = O, S, NR26, C(R27)R28; E, G, J, L = N, CR29; R20-R23, R26-R29 = H, OH, lower alkoxy, each (un)substituted lower alkyl, cycloalkyl, aryl, arylalkyl, aromatic heterocyclyl, aromatic heterocyclylalkyl, nonarom. heterocyclyl, lower alkenyl, lower alkylidene, NH2, or CONH2, CO2H, lower alkoxycarbonyl, lower alkenyloxycarbonyl, aryl-lower alkoxycarbonyl, aromatic heterocyclyl-lower alkoxycarbonyl, lower alkylcarbonylamino, oxo; R24, R25 = H, each (un)substituted lower alkyl, cycloalkyl, or nonarom. heterocyclyl] are prepared These compds. have an excellent effect of proliferating human c-Mpl-Ba/F3 cells and an activity of increasing platelets (thrombocytosis) based on the effect of promoting the formation of megakaryocytic colonies and are useful in treating thrombopenia. Thus, 2.1 mL Et isonipecotinate was added to a solution of 750 mg 5,6-dichloro-N-[4-(4-chlorothiophen-2-yl)-5-(4-cyclohexylpiperazin-1- yl)thiazol-2-yl]nicotinamide in 10 mL THF, heated to 50°, and stirred for 5 h to give, after workup and silica gel chromatog., 881 mg 1-[3-chloro-5-[[4-(4-chlorothiophen-2-yl)-5-(4-cyclohexylpiperazin-1-yl)thiazol-2-yl]carbamoyl]-2-pyridyl]piperidine-4-carboxylic acid Et ester which (30 mg) was dissolved in 1 mL MeOH, treated with 0.12 mL 1 M aqueous NaOH solution at room temperature, stirred for 24 h, distilled under reduced pressure, dissolved in EtOAc, treated with 0.2 mL 1 M aqueous HCl solution, stirred, and distilled under reduced pressure, followed by washing the residue with Et2O to give 20 mg 1-[3-chloro-5-[[4-(4-chlorothiophen-2-yl)-5-(4-

cyclohexylpiperazin-1-yl)thiazol-2-yl]carbamoyl]-2-pyridyl]piperidine-4-carboxylic acid hydrochloride (II). II and recombinant human thrombopoietin (rhTPO) at 2.4 ad 0.012 nM, resp., showed 30% of the maximum cell proliferating effect of each compound tested on human c-Mpl-Ba/F3 cell.

IC ICM C07D417-04
ICS C07D417-14; C07D453-02; C07D277-44; A61K031-439; A61K031-4545; A61K031-4709; A61K031-496; A61K031-506; A61K031-5377; A61K031-538; A61K031-695; A61K031-498; A61K031-55; A61K031-426; A61P007-00; A61P043-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 570403-00-8P 570403-01-9P 570403-02-0P 570403-03-1P 570403-05-3P
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570405-61-7P 570405-62-8P 570405-63-9P 570405-64-0P 570405-65-1P

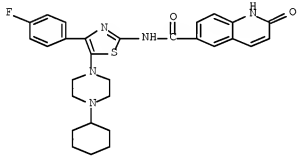
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of 2-acylaminothiazole derivs. or salts thereof as c-Mpl receptor ligands for proliferating human c-Mpl-Ba/F3 cells and increasing platelets via promoting the formation of megakaryocytic colony)

IT 570405-03-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-acylaminothiazole derivs. or salts thereof as c-Mpl receptor ligands for proliferating human c-Mpl-Ba/F3 cells and increasing platelets via promoting the formation of megakaryocytic colony)

RN 570405-03-7 HCAPLUS

CN 6-Quinolinecarboxamide, N-[5-(4-cyclohexyl-1-piperazinyl)-4-(4-fluorophenyl)-2-thiazolyl]-1,2-dihydro-2-oxo-, hydrochloride (1:?) (CA INDEX NAME)



●x HCl

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 13 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:117785 HCAPLUS Full-text

DOCUMENT NUMBER: 138:170073

TITLE: Preparation of N-[2-[3-[(4-aminomethyl)phenyl]propylamino]ethyl]amides as human β-tryptase inhibitors for treatment of respiratory diseases, allergic diseases, inflammatory intestinal diseases, hyperprolliferative skin diseases, vascular edema, and rheumatoid arthritis

INVENTOR(S): Kato, Yutaka; Miyazaki, Yutaka; Shimada, Hiroyasu; Manabe, Tadashi; Shiromizu, Ikuya; Okamoto, Atsushi

PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

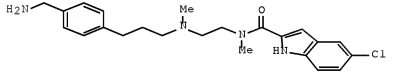
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011812	A1	20030213	WO 2002-JP7843	20020801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2456096	A1	20030213	CA 2002-2456096	20020801
AU 2002323746	A1	20030217	AU 2002-323746	20020801
EP 1445250	A1	20040811	EP 2002-755745	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20050043304	A1	20050224	US 2004-485331	20040130
PRIORITY APPLN. INFO.:			JP 2001-233818 A	20010801
			WO 2002-JP7843 W	20020801

OTHER SOURCE(S): MARPAT 138:170073
ED Entered STN: 14 Feb 2003
GI



I

AB The title amides with general formula of R1R2NCH2-A-CH2CH2CH2NR3CH2CH2NR4-X-B [wherein R1, R2, and R3 = independently H, (un)substituted alkyl, alkenyl, alkynyl, or acyl; or R1 and R2 together form 5-6 membered ring with the nitrogen atom attached; R4 = H or alkyl; A = (un)substituted 5-6 membered (hetero)aromatic ring; B = (un)substituted (hetero)cyclyl, with exclusions; X = CO, SO2, CH2, COCH=CH, SO2CH=CH, COCH2O, or SO2CH2O] and pharmaceutically acceptable salts thereof are prepared as human β-tryptase inhibitors, with a high absorbability, a low toxicity, and an extremely high selectivity. For example, the amide I•2HCl was prepared in a 5-step synthesis comprising coupling reaction of 5-chloroindole-2-carboxylic acid with the corresponding amine (prepn given). I•2HCl showed IC50 of 0.001 μM against β-tryptase. The title amides are useful for the treatment of respiratory diseases, allergic diseases, inflammatory intestinal diseases, hyperprolliferative skin diseases, vascular edema, and rheumatoid arthritis (no data). Formulations containing the target compds. as an active ingredient were also described.

IC ICM C07C211-30
ICS C07C311-14; C07C311-18; C07C233-78; C07C235-50; C07C235-10; C07C235-66; A61K031-137; A61K031-166; A61K031-18; A61K031-381; A61K031-428; A61K031-47; A61K031-472; A61P001-00; A61P009-00; A61P011-00; A61P011-06; A61P017-00; A61P027-14

CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 25, 63

IT 496944-44-6P 496944-45-7P 496944-46-8P 496944-47-9P 496944-48-0P

496944-50-4P 496944-51-5P 496944-52-6P 496944-53-7P 496944-54-8P
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496945-36-9P 496945-37-0P 496945-38-1P 496945-39-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human β-tryptase inhibitor; Preparation of [[[(aminomethyl)phenyl]propylamino]ethyl]amides by coupling reaction as human β-tryptase inhibitors)

IT 496945-40-5P 496945-41-6P 496945-42-7P 496945-43-8P 496945-44-9P
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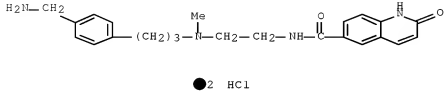
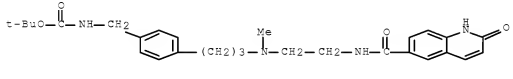
496946-70-4P 496946-71-5P 496946-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; Preparation of [[[(aminomethyl)phenyl]propylamino]ethyl]amides by coupling reaction as human β-tryptase inhibitors)

IT 496945-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human β-tryptase inhibitor; Preparation of [[[(aminomethyl)phenyl]propylamino]ethyl]amides by coupling reaction as human β-tryptase inhibitors)

RN 496945-29-0 HCAPLUS
CN 6-Quinolinecarboxamide, N-[2-[[3-[4-(aminomethyl)phenyl]propyl]methylamino]ethyl]-1,2-dihydro-2-oxo-, hydrochloride (1:2) (CA INDEX NAME)



IT 496946-59-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; Preparation of [[[(aminomethyl)phenyl]propylamino]ethyl]amides by coupling reaction as human β-tryptase inhibitors)
RN 496946-59-9 HCAPLUS
CN Carbamic acid, [[4-[3-[[2-[[(1,2-dihydro-2-oxo-6-quinolinyl)carbonyl]amino]ethyl]methylamino]propyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 14 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:793427 HCAPLUS Full-text
DOCUMENT NUMBER: 137:310932
TITLE: Preparation of N-substituted nonaryl heterocyclyl amides as NMDA/NR2B antagonists for relieving pain
INVENTOR(S): Liverton, Nigel J.; Butcher, John W.; McIntyre, Charles J.; Claiborne, Christopher F.; Claremon, David A.; McCauley, James A.; Romano, Joseph J.; Thompson, Wayne; Munson, Peter M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080928	A1	20021017	WO 2002-US10269	20020402

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2443108	A1	20021017	CA 2002-2443108		20020402
AU 2002338334	A1	20021021	AU 2002-338334		20020402
AU 2002338334	B2	20080814			
US 20030119811	A1	20030626	US 2002-114685		20020402
US 7259157	B2	20070821			
EP 1390034	A1	20040225	EP 2002-763896		20020402
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JP 2005511478 T		20050428	JP 2002-578967		20020402
PRIORITY APPLN. INFO.:			US 2001-281166P	P	20010403
			WO 2002-US10269	W	20020402

OTHER SOURCE(S): MARPAT 137:310932

ED Entered STN: 18 Oct 2002

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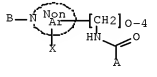

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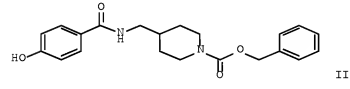

II

AB The title compds. [I; NonAr = nonarom. 5-7 membered containing heteroatoms; A = (un)substituted Ph, pyrrolyl, imidazolyl, etc.; B = aryl(CH2)0-3(CH2)0-2CO, heteroaryl(CH2)1-3O(CH2)0-2CO, etc.; X = H, OH, F, etc.] which are effective as NMDA NR2B antagonists useful for relieving pain, were prepared E.g., a 2-step synthesis of II, starting with 4-aminomethylpiperidine, was given. The compds. I exhibit IC50's of less than 50 μM in the FLIPR and binding assays, and thus they have been found to exhibit biol. activity as NMDA NR2B antagonists.

IC ICM A61K031-55

ICS A61K031-54; A61K031-535; A61K031-505; A61K031-52; A61K031-495; A61K031-47; A61K031-44; A61K031-445; A61K031-42; A61K031-415; A61K031-425; A61K031-41; C07D223-04; C07D239-02; C07D241-02; C07D267-02; C07D401-12; C07D403-12; C07D405-12

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 471250-99-4P 471251-00-0P 471251-01-1P 471251-02-2P 471251-03-3P

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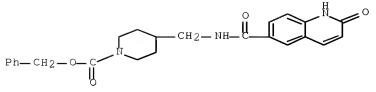
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-substituted nonaryl heterocyclyl amides as NMDA/NR2B antagonists for relieving pain)

IT 471252-17-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-substituted nonaryl heterocyclyl amides as NMDA/NR2B antagonists for relieving pain)

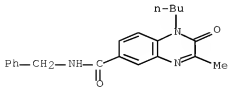
RN 471252-17-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[(1,2-dihydro-2-oxo-6-quinolinyl)carbonyl]amino]methyl]-, phenylmethyl ester (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 15 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:338061 HCAPLUS Full-text
DOCUMENT NUMBER: 137:310892
TITLE: Solid-phase synthesis of 'diverse' heterocycles
AUTHOR(S): Purandare, Ashok V.; Gao, Aiming; Poss, Michael A.
CORPORATE SOURCE: New Leads Chemistry, Bristol-Myers Squibb PRI, Princeton, NJ, 08543, USA
SOURCE: Tetrahedron Letters (2002), 43(21), 3903-3906
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:310892
ED Entered STN: 07 May 2002
AB Diverse heterocycles, i.e., quinoxalinediones, quinoxalinones, benzimidazolones, and benzimidazoles, were prepared from 4-fluoro-3-nitrobenzoic acid by solid-phase synthesis on polymer-supported aminomethylphenol.
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 471891-36-8P 471891-38-0P 471891-40-4P 471891-42-6P 471891-44-8P
471891-46-0P 471891-48-2P 471891-50-6P 471891-52-8P
471891-54-0P 471891-55-1P 471891-56-2P 471891-57-3P 471891-58-4P
471891-59-5P 471891-60-8P 471891-61-9P 471891-62-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of quinoxalinediones, quinoxalinones, benzimidazolones, and benzimidazoles)
IT 471891-46-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of quinoxalinediones, quinoxalinones, benzimidazolones, and benzimidazoles)
RN 471891-46-0 HCAPLUS
CN 6-Quinoxalinecarboxamide, 1-butyl-1,2-dihydro-3-methyl-2-oxo-N-(phenylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 16 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:476381 HCAPLUS Full-text
DOCUMENT NUMBER: 135:100164
TITLE: (R)-1-{(2-Oxo-1,2-dihydroquinolin-6-yl)[3-(trifluoromethyl)phenyl]methyl}-1H-1,2,4-triazol-4-ium bromide
AUTHOR(S): Peeters, Oswald M.; Blaton, Norbert M.; De Ranter, Camiel J.
CORPORATE SOURCE: Faculteit Farmaceutische Wetenschappen, Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2001), E57(7), o655-o656
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/issues/2001/07/00/ya6033/ya6033.pdf
PUBLISHER: International Union of Crystallography
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
ED Entered STN: 03 Jul 2001
AB The metabolism of all-trans-retinoic acid is mediated by a cytochrome dependent P 450 system. The title compound, C19H14F3N4O+·Br- (R111214), is an inhibitor of P 450. The three planar ring systems, viz. the triazolyl, Ph and quinolinone groups, are arranged in a propeller-like fashion around the central CH group. The dihedral angles formed by the triazolyl/phenyl, triazolyl/quinolinone and phenyl/quinolinone planes are 55.8(1), 79.85(9) and 78.49(9)°, resp. The N-H...O H bonds, involving the triazolium N-H group and the quinolinone O atom, link the cations into infinite chains stretching along the c axis of the crystal. Crystallog. data are given.
CC 75-8 (Crystallography and Liquid Crystals)
Section cross-reference(s): 1, 27, 63
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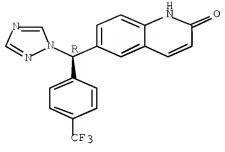
RL: PRP (Properties)
(crystal structure of)
IT 349553-99-7
RL: PRP (Properties)
(crystal structure of)
RN 349553-99-7 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(R)-1H-1,2,4-triazol-1-yl[4-(trifluoromethyl)phenyl]methyl]-, hydrobromide (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HBr

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 17 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:260270 HCAPLUS Full-text
DOCUMENT NUMBER: 132:293680
TITLE: Preparation of tetrahydrobenzazepine derivatives as modulators of dopamine D3 receptors (antipsychotic agents)
INVENTOR(S): Hadley, Michael Stewart; Johnson, Christopher Norbert; MacDonald, Gregor James; Stemp, Geoffrey; Vong, Antonio Kuok Keong
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021951	A1	20000420	WO 1999-EP7763	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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BR 9914370	A	20011127	BR 1999-14370	19991006
HU 2001004280	A2	20020328	HU 2001-4280	19991006
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JP 2002527433	T	20020827	JP 2000-575857	19991006
AU 761018	B2	20030529	AU 2000-10381	19991006
NZ 511018	A	20030926	NZ 1999-511018	19991006

AT 316969	T	20060215	AT 1999-953833		19991006
ES 2255311	T3	20060616	ES 1999-953833		19991006
IN 2001MN00358	A	20050304	IN 2001-MN358		20010403
ZA 2001002758	A	20020604	ZA 2001-2758		20010404
NO 2001001745	A	20010606	NO 2001-1745		20010406
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BG 105467	A	20011130	BG 2001-105467		20010424
US 6605607	B1	20030812	US 2001-806902		20010716
PRIORITY APPLN. INFO.:			GB 1998-21976	A	19981008
			GB 1998-24340	A	19981106
			GB 1999-10711	A	19990507
			GB 1999-18032	A	19990730
			WO 1999-EP7763	W	19991006

OTHER SOURCE(S): MARPAT 132:293680
ED Entered STN: 21 Apr 2000
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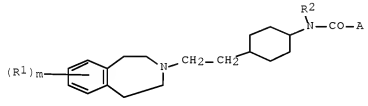

I

AB The title compds. I [R1 represents a hydrogen or halogen atom, hydroxy,, etc.; R2 represents a hydrogen atom or a C1-4alkyl group; m is 1 or 2; A represents Ar, etc.; (Ar represents an optionally substituted Ph ring or an optionally substituted 5- or 6-membered aromatic heterocyclic ring; or an optionally substituted bicyclic ring system)] are prepared In binding expts. on cloned dopamine receptors, compds. of this invention had pKi values in the range 7 - 9. Formulations are given.

IC ICM C07D401-12
ICS C07D403-12; A61K031-55; C07D223-16; C07D471-04; C07D413-12; C07D405-12; C07D409-12; C07D417-12

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63

IT 264262-48-8P 264262-49-9P 264262-50-2P 264262-51-3P 264262-52-4P
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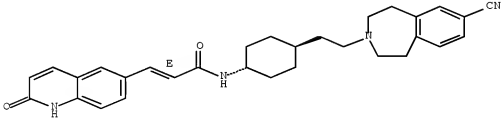
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydrobenzazepine derivs. as modulators of dopamine D3 receptors (antipsychotic agents))

IT 264262-65-9P 264263-39-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydrobenzazepine derivs. as modulators of dopamine D3 receptors (antipsychotic agents))

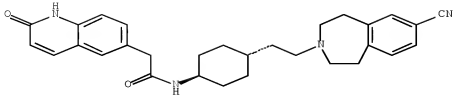
RN 264262-65-9 HCAPLUS
CN 2-Propenamide, N-[trans-4-[2-(7-cyano-1,2,4,5-tetrahydro-3H-3-benzazepin-3-yl)ethyl]cyclohexyl]-3-(1,2-dihydro-2-oxo-6-quinolinyl)-, (2E)- (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



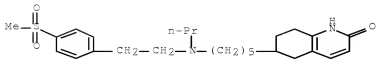
RN 264263-39-0 HCAPLUS
CN 6-Quinolineacetamide, N-[trans-4-[2-(7-cyano-1,2,4,5-tetrahydro-3H-3-benzazepin-3-yl)ethyl]cyclohexyl]-1,2-dihydro-2-oxo- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 18 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:209095 HCAPLUS Full-text
DOCUMENT NUMBER: 132:334349
TITLE: Synthesis and dopaminergic activity of heterocyclic analogues of 5,6-dihydroxy-2-aminotetralins
AUTHOR(S): Bosch, Joan; Roca, Tomas; Perez, Carles G.; Montanari, Stefania
CORPORATE SOURCE: Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona, Barcelona, 08028, Spain
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(6), 563-566
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 Mar 2000
AB Heterocyclic analogs of 5,6-dihydroxy-2-aminotetralins were synthesized and their in-vitro dopaminergic activity was compared to that of (-)-2-(diisopropylamino)-5,6-dihydroxytetralin (I) and the novel potent agonist Z12571. The results show that changing the catechol ring for a heterocycle decreases the D1-like activity of the target mols. However, the D2-like activity of a newly prepared tetrahydroquinoline was comparable to that of I.
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 268543-57-3P 268543-58-4P 268543-59-5P 268543-60-8P 268543-61-9P 268543-62-0P 268543-63-1P 268543-64-2P 268543-65-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and dopaminergic activity of heterocyclic analogs of hydroxyaminotetralin)
IT 268543-65-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and dopaminergic activity of heterocyclic analogs of hydroxyaminotetralin)
RN 268543-65-3 HCAPLUS
CN 2(1H)-Quinolinone, 5,6,7,8-tetrahydro-6-[5-[[2-[4-(methylsulfonyl)phenyl]ethyl]propylamino]pentyl]- (CA INDEX NAME)

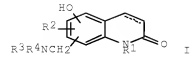


REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 19 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:139831 HCAPLUS Full-text
DOCUMENT NUMBER: 130:182369
TITLE: Preparation of carbostyril derivatives for inhibiting skin erythema and/or skin pigmentation.
INVENTOR(S): Oshiro, Yasuo; Nishi, Takao; Kuwahara, Keiichi; Watanabe, Kozo
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909011	A1	19990225	WO 1998-JP3657	19980818
W: AU, BR, CA, CN, ID, KR, MX, SG, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IN 1998CA01253	A	20050311	IN 1998-CA1253	19980717
TW 436483	B	20010528	TW 1998-87112066	19980723
EG 24161	A	20080820	EG 1998-942	19980813
JP 11124366	A	19990511	JP 1998-230407	19980817
CA 2297439	A1	19990225	CA 1998-2297439	19980818
CA 2297439	C	20061219		
AU 9886500	A	19990308	AU 1998-86500	19980818
AU 725464	B2	20001012		
EP 1005458	A1	20000607	EP 1998-937851	19980818
EP 1005458	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9811307	A	20000829	BR 1998-11307	19980818
CN 1141298	C	20040310	CN 1998-808277	19980818
AT 279395	T	20041015	AT 1998-937851	19980818
PT 1005458	T	20050131	PT 1998-937851	19980818
ES 2232001	T3	20050516	ES 1998-937851	19980818
US 6133264	A	20001017	US 2000-485454	20000210
MX 200001440	A	20001230	MX 2000-1440	20000210
HK 1029346	A1	20040820	HK 2001-100255	20010111
PRIORITY APPLN. INFO.:			JP 1997-222431 A	19970819
			WO 1998-JP3657 W	19980818

OTHER SOURCE(S): MARPAT 130:182369
ED Entered STN: 04 Mar 1999
GI



AB Title compds. [I; R1 = H, alkyl, alkenyl; R2 = H, alkyl, alkoxy, alkenyloxy, alkenyl, tetrahydropyranyloxy; R3, R4 = alkyl, hydroxalkyl; R3R4N = (substituted) 5-6 membered saturated heterocyclyl; dotted line = optional double bond; with provisos], were prepared Thus, 5-acetoxy-3,4-dihydro-8-methoxy-2(1H)-quinolinone, Me2NH, and aqueous H2CO were refluxed 10 h in EtOH to give 6-dimethylaminomethyl-3,4-dihydro-5-hydroxy-8-methoxy-2(1H)-quinolinone hydrochloride. I as 3% solns. on guinea pigs gave 38-78% inhibition of sunburn. I formulations are given.

IC ICM C07D215-26
ICS A61K031-47; C07D215-22; C07D405-12

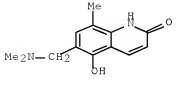
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 62, 63

IT 141498-71-7P 148934-13-8P 156937-60-9P 220687-63-8P
220687-64-9P 220687-65-0P 220687-67-2P 220687-68-3P 220687-69-4P
220687-70-7P 220687-71-8P 220687-74-1P 220687-75-2P 220687-77-4P
220687-78-5P 220687-80-9P 220687-81-0P 220687-82-1P 220687-83-2P
220687-84-3P 220687-85-4P 220687-86-5P 220687-87-6P 220687-88-7P
220687-89-8P 220687-91-2P 220687-92-3P 220687-94-5P 220687-95-6P
220687-96-7P 220687-97-8P 220687-98-9P 220687-99-0P 220688-00-6P
220688-02-8P 220688-03-9P 220688-04-0P 220688-05-1P 220688-06-2P
220688-07-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyril derivs. for inhibiting skin erythema and/or skin
pigmentation)

IT 156937-60-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyril derivs. for inhibiting skin erythema and/or skin
pigmentation)

RN 156937-60-9 HCAPLUS

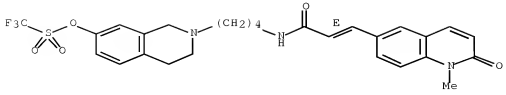
CN 2(1H)-Quinolinone, 6-[(dimethylamino)methyl]-5-hydroxy-8-methyl- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

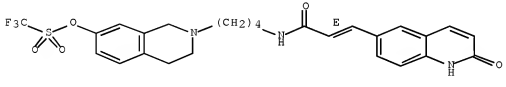
L88 ANSWER 20 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:118513 HCAPLUS Full-text
DOCUMENT NUMBER: 130:306029
TITLE: Novel 1,2,3,4-tetrahydroisoquinolines with high affinity and selectivity for the dopamine D3 receptor
AUTHOR(S): Austin, Nigel E.; Avenell, Kim Y.; Boyfield, Izzy; Branch, Clive L.; Coldwell, Martyn C.; Hadley, Michael S.; Jeffrey, Phillip; Johns, Amanda; Johnson, Christopher N.; Nash, David J.; Riley, Graham J.; Smith, Stephen A.; Stacey, Rachel C.; Stemp, Geoffrey; Thewlis, Kevin M.; Vong, Antonio K. K.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(2), 179-184
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Feb 1999
AB Using clearance and brain penetration studies as a screen, a tetrahydroisoquinoline (I) was identified as a lead having low clearance in rats (CLb 20 mL/min/kg). Introduction of a 7-CF3SO2O- substituent into the tetrahydroisoquinoline, followed by replacement of the biphenylamido group of I by a 3-indolylpropenamido group gave a compound having high D3 receptor affinity (pKi 8.4) and 150 fold selectivity over the D2 receptor.
CC 1-3 (Pharmacology)
Section cross-reference(s): 27
IT 199676-77-2P 199677-14-0P 199677-31-1P 199677-33-3P 199677-35-5P 199677-80-0P 203504-70-5P 203504-73-8P 203504-76-1P 203504-79-4P 203504-85-2P 203504-87-4P 203504-89-6P 203504-90-9P 203504-91-0P 203504-94-3P 203505-23-1P 223566-71-0P 223566-76-5P 223566-78-7P 223566-80-1P 223566-91-4P 223567-07-5P 223567-09-7P 223567-12-2P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(novel tetrahydroisoquinolines with high affinity and selectivity for dopamine D3 receptor over the D2 receptor in relation to structure and pharmacokinetics)
IT 223567-09-7P 223567-12-2P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(novel tetrahydroisoquinolines with high affinity and selectivity for dopamine D3 receptor over the D2 receptor in relation to structure and pharmacokinetics)
RN 223567-09-7 HCAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, 2-[4-[[(2E)-3-(1,2-dihydro-1-methyl-2-oxo-6-quinolinyl)-1-oxo-2-propen-1-yl]amino]butyl]-1,2,3,4-tetrahydro-7-isoquinolinyl ester (CA INDEX NAME)

Double bond geometry as shown.



RN 223567-12-2 HCAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-,
2-[4-[[(2E)-3-(1,2-dihydro-2-oxo-6-quinolinyl)-1-oxo-2-propen-1-yl]amino]butyl]-1,2,3,4-tetrahydro-7-isoquinolinyl ester (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib ed abs hitind hitstr 21-39
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX' - CONTINUE? (Y)/N:y

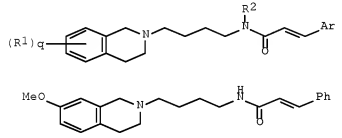
L88 ANSWER 21 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:126237 HCAPLUS Full-text
DOCUMENT NUMBER: 128:192564
ORIGINAL REFERENCE NO.: 128:38043a,38046a
TITLE: Tetrahydroisoquinoline derivatives and their pharmaceutical use as dopamine D3 receptor modulators
INVENTOR(S): Nash, David John; Stemp, Geoffrey
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK; Nash, David John; Stemp, Geoffrey
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806699	A1	19980219	WO 1997-EP4408	19970808
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,				

UZ, VN, YU, ZW
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2263284	A1	19980219	CA 1997-2263284		19970808
AU 9742046	A	19980306	AU 1997-42046		19970808
EP 922035	A1	19990616	EP 1997-940074		19970808
EP 922035	B1	20010207			
R: BE, CH, DE, ES, FR, GB, IT, LI, NL					
JP 2000517301	T	20001226	JP 1998-509410		19970808
ES 2154470	T3	20010401	ES 1997-940074		19970808
ZA 9707191	A	19990315	ZA 1997-7191		19970812
IN 1997DE02297	A	20050311	IN 1997-DE2297		19970814
US 6143762	A	20001107	US 1999-242200		19990211
PRIORITY APPLN. INFO.:			GB 1996-17079	A	19960814
			GB 1997-4523	A	19970305
			WO 1997-EP4408	W	19970808

OTHER SOURCE(S): MARPAT 128:192564
ED Entered STN: 02 Mar 1998
GI



AB Title compds. I and their salts are claimed [wherein R1 = H, halo, OH, cyano, NO2, CF3, CF3O, CF3SO2O, alkyl, alkoxy, arylalkoxy, alkylthio, alkoxyalkyl, alkanoyl, alkoxycarbonyl, alkylsulfonyl, alkylsulfonyloxy, alkylsulfonylalkyl, arylsulfonyl, alkylamido, aroyl, etc., or group Ar1Z, wherein Ar1 = (un)substituted Ph ring or (un)substituted 5- or 6-membered aromatic heterocyclic ring and Z = bond, O, S, or CH2; R2 = H, alkyl; q = 1, 2; Ar = (un)substituted Ph, 5- or 6-membered aromatic heterocyclic ring, or bicyclic aromatic or heteroarom. ring system]. The compds. have affinity for dopamine receptors, in particular the D3 receptor, and thus are potentially useful in the treatment of conditions wherein modulation of the D3 receptor is beneficial, e.g., as antipsychotic or antiparkinsonian agents. For example, amidation of trans-cinnamic acid with 2-(4-aminobutyl)-7-methoxy-1,2,3,4-tetrahydroisoquinoline (preparation given) using EDC and HOBT in CH2Cl2 gave 68% title compound II. In an assay for binding at cloned human dopamine D3 receptors in vitro, compds. I had pKi values of 7.0-9.0.

IC ICM C07D217-04
ICS A61K031-47; C07D405-12; C07D401-12; C07D417-12; C07D471-04; C07D471-04; C07D221-00; C07D209-00
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 203504-70-5P 203504-71-6P 203504-73-8P 203504-74-9P 203504-75-0P

203504-76-1P 203504-77-2P 203504-78-3P 203504-79-4P 203504-80-7P
203504-81-8P 203504-82-9P 203504-83-0P 203504-84-1P 203504-85-2P
203504-86-3P 203504-87-4P 203504-88-5P 203504-89-6P 203504-90-9P
203504-91-0P 203504-92-1P 203504-93-2P 203504-94-3P 203504-96-5P
203504-97-6P 203504-98-7P 203504-99-8P 203505-00-4P 203505-02-6P
203505-03-7P 203505-04-8P 203505-05-9P 203505-06-0P 203505-07-1P
203505-08-2P 203505-09-3P 203505-10-6P 203505-11-7P 203505-12-8P
203505-13-9P 203505-14-0P 203505-15-1P 203505-16-2P 203505-17-3P
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203505-41-3P 203505-42-4P 203505-43-5P 203505-44-6P 203505-45-7P
203505-46-8P 203505-47-9P 203505-48-0P 203505-49-1P
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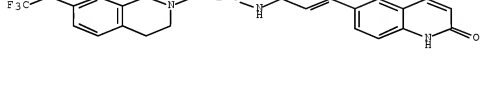
203505-56-0P 203505-57-1P 203505-58-2P 203505-59-3P 203505-60-6P
203505-61-7P 203505-62-8P 203505-63-9P 203505-64-0P 203505-65-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydroisoquinoline derivs. as dopamine D3 receptor modulators)

IT 203505-48-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydroisoquinoline derivs. as dopamine D3 receptor modulators)

RN 203505-48-0 HCAPLUS

CN 2-Propenamide, 3-(1,2-dihydro-2-oxo-6-quinolinyl)-N-[4-[3,4-dihydro-7-(trifluoromethoxy)-2(1H)-isoquinolinyl]butyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

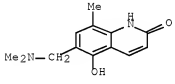
L88 ANSWER 22 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:534101 HCAPLUS Full-text
DOCUMENT NUMBER: 121:134101
ORIGINAL REFERENCE NO.: 121:24249a,24252a
TITLE: Preparation of quinoline derivative or salt thereof and remedy for cardiac diseases containing the same
INVENTOR(S): Kyotani, Yoshinori; Ogiya, Tadaaki; Toma, Tsutomu; Kurihara, Yuji; Kitamura, Takahiro; Yamaguchi, Takashi; Onogi, Kazuhiro; Sato, Seichi; Shigyo, Hiromichi; et al.
PATENT ASSIGNEE(S): Kowa Co., Ltd., Japan
SOURCE: PCT Int. Appl., 265 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9322317	A1	19931111	WO 1993-JP566	19930428
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 638571	A1	19950215	EP 1993-911951	19930428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 3406600	B2	20030512	JP 1993-519131	19930428
US 5576324	A	19961119	US 1994-325270	19941027
PRIORITY APPLN. INFO.:			JP 1992-112862 A	19920501
			WO 1993-JP566 W	19930428

OTHER SOURCE(S): MARPAT 121:134101
ED Entered STN: 17 Sep 1994
GI For diagram(s), see printed CA Issue.
AB Quinoline derivs. [I; ring A = a furan, dihydrofuran or dioxolane ring; R1 = OH, CO2H, alkoxycarbonyl, CONH2, alkenyl, CHO, cyano, (un)substituted alkyl, C(:NR10)R9; R9 = NH2, alkyl; R10 = H, OH; R2 = H, (un)substituted alkyl, alkenyl, acyl, OH; R3, R4 = H, halo, (un)substituted alkyl or NH2, alkoxy, alkylthio, CO2H, alkoxycarbonyl, acyl, CONH2, cyano, NO2; R5, R6, R7, R8 = H or alkyl; m = an integer 0-3; symbol.....means that there may be a double bond formed by R6 and R8] and medicinally acceptable salts are prepared The compds. I have a pos. inotropic effect on myocardia and an antiarrhythmic effect and can dilate blood vessels without extremely increasing the heart rate. Therefore, a remedy for cardiac diseases containing I as the active ingredient is remarkably useful for treating cardiac insufficiency and arrhythmia and as vasodilators and carditonics. Thus, 5-hydroxy-6-allyl-8-methylcarbostyryl was stirred with m-chloroperbenzoic acid in CHCl3 at 50° for 17 h to give a tetrahydrofuroquinolinone derivative (II; X = OH, R9 = H) which was mesylated by MeSO2Cl in pyridine and underwent azidolysis with NaN3 DMF at 100° to give, after hydrogenation over 10% Pd-C, II (X = NH2, R11 = H). II.HCl (X = NH2, R11 = Me) at 100 mg/kg p.o. inhibited the CHCl3-induced arrhythmia in mice by 100%.
IC ICM C07D491-048
ICS C07D491-056; A61K031-47
CC 28-5 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 124-02-7P, Diallylamine 5187-82-6P 19315-93-6P 55044-94-5P
59557-92-5P, 6-Bromo-3-methoxyaniline 75785-11-4P 141498-72-8P
143268-85-3P 143268-86-4P 153999-60-1P 153999-67-8P 156936-85-5P
156936-86-6P 156936-87-7P 156936-88-8P 156936-89-9P 156936-90-2P
156936-91-3P 156936-92-4P 156936-94-6P 156936-96-8P 156936-98-0P
156936-99-1P 156937-00-7P 156937-01-8P 156937-02-9P 156937-03-0P
156937-04-1P 156937-05-2P 156937-06-3P 156937-07-4P 156937-08-5P
156937-09-6P 156937-10-9P 156937-11-0P 156937-12-1P 156937-13-2P
156937-14-3P 156937-16-5P 156937-17-6P 156937-18-7P 156937-19-8P
156937-20-1P 156937-21-2P 156937-23-4P 156937-24-5P 156937-25-6P
156937-26-7P 156937-27-8P 156937-28-9P 156937-29-0P 156937-30-3P
156937-31-4P 156937-32-5P 156937-33-6P 156937-34-7P 156937-35-8P
156937-36-9P 156937-37-0P 156937-38-1P 156937-39-2P 156937-40-5P
156937-41-6P 156937-42-7P 156937-43-8P 156937-44-9P 156937-47-2P
156937-48-3P 156937-51-8P 156937-52-9P 156937-53-0P 156937-54-1P
156937-55-2P 156937-56-3P 156937-57-4P 156937-58-5P 156937-59-6P
156937-60-9P 156937-61-0P 156937-62-1P 156937-63-2P
156937-64-3P 156937-65-4P 156937-66-5P 156937-67-6P 156937-68-7P
156937-69-8P 156937-70-1P 156937-71-2P 156937-72-3P
RL: SPN (Synthetic preparation); PREP (Preparation)

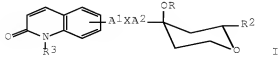
(preparation of, as intermediate for quinoline derivative medicament for cardiac
diseases)
IT 156937-60-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for quinoline derivative medicament for cardiac
diseases)
RN 156937-60-9 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(dimethylamino)methyl]-5-hydroxy-8-methyl- (CA INDEX NAME)



L88 ANSWER 23 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:270138 HCAPLUS Full-text
DOCUMENT NUMBER: 120:270138
ORIGINAL REFERENCE NO.: 120:47851a,47854a
TITLE: Ether-containing oxoquinolinone inhibitors of 5-lipoxygenase
INVENTOR(S): Dellaria, Joseph F.; Moore, Jimmie L.; Brooks, Dee W.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5268379	A	19931207	US 1992-935079	19920824
WO 9404528	A1	19940303	WO 1993-US6914	19930723
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5350765	A	19940927	US 1993-113942	19930830

PRIORITY APPLN. INFO.: US 1992-935079 A 19920824
OTHER SOURCE(S): MARPAT 120:270138
ED Entered STN: 28 May 1994
GI



AB The title compds. I [A1 = propynyl, CH2, valence bond; A2 = (un)substituted 1,3-propanediyl, (un)substituted 1,3-propynediyl, etc.; R1 = C1-4 alkyl; R2, R3 = H, C1-4 alkyl; X = O, S, SO2, NR4; R4 = H, C1-4 alkyl], which inhibit 5-lipoxygenase enzyme activity (no data) and are useful in the treatment of allergic (no data) and inflammatory diseases in which leukotrienes play a role, are prepared Thus, 4-methoxy-4-[3-[(1,2-dihydro-1-methyl-2-oxoquinoline-6-yl)methoxy]-trans- prop-1-enyl]-2-methyltetrahydropyran was prepared from 2-methyltetrahydro-4H-pyran-4-one in 4 steps.

IC ICM C07D405-12
ICS A61K031-47

INCL 514312000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

IT 153950-20-0 153950-20-0 153950-21-1 153950-22-2 153950-25-5
153950-30-2 153950-31-3 153950-34-6 153950-35-7 153950-37-9
153950-38-0 153950-40-4 153950-41-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as intermediate in preparation of lipoxygenase inhibitors)

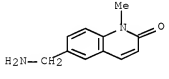
IT 153950-19-7 153950-23-3 153950-24-4 153950-26-6 153950-27-7
153950-28-8 153950-29-9 153950-32-4 153950-33-5 153950-36-8
153950-39-1 153950-42-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as lipoxygenase inhibitor)

IT 91-60-1, 2-Naphthalenethiol 939-26-4, 2-(Bromomethyl)naphthalene
1193-20-0, 2-Methyltetrahydro-4H-pyran-4-one 2018-90-8,
2-Aminomethylnaphthalene 2567-29-5 6089-04-9 29768-03-4,
3-(Pyrid-2-yl)prop-2-ynol 29943-42-8, Tetrahydro-4H-pyran-4-one
57188-99-5, Tetrahydro-2-(1-methyl-2-propynyloxy)-2H-pyran 131610-09-8,
1,2-Dihydro-1-methyl-2-oxo-6-(bromomethyl)quinoline 153950-20-0
153950-40-4, (1,2-Dihydro-1-methyl-2-oxoquinoline-6-yl)methylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant, in preparation of lipoxygenase inhibitors)

IT 153950-40-4 153950-41-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as intermediate in preparation of lipoxygenase inhibitors)

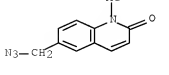
RN 153950-40-4 HCAPLUS

CN 2(1H)-Quinolinone, 6-(aminomethyl)-1-methyl- (CA INDEX NAME)



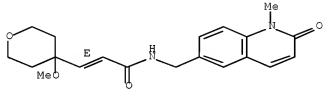
RN 153950-41-5 HCAPLUS

CN 2(1H)-Quinolinone, 6-(azidomethyl)-1-methyl- (CA INDEX NAME)

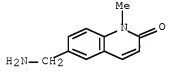


IT 153950-39-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as lipoxygenase inhibitor)
RN 153950-39-1 HCAPLUS
CN 2-Propenamide, N-[(1,2-dihydro-1-methyl-2-oxo-6-quinolinyl)methyl]-3-(tetrahydro-4-methoxy-2H-pyran-4-yl)-, (E)- (9CI) (CA INDEX NAME)

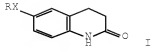
Double bond geometry as shown.



IT 153950-40-4, (1,2-Dihydro-1-methyl-2-oxoquinoline-6-yl)methylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant, in preparation of lipoxygenase inhibitors)
RN 153950-40-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-(aminomethyl)-1-methyl- (CA INDEX NAME)



L88 ANSWER 24 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:106055 HCAPLUS Full-text
DOCUMENT NUMBER: 116:106055
ORIGINAL REFERENCE NO.: 116:17950h,17951a
TITLE: 3,4-Dihydroquinolin-2(1H)-ones as combined inhibitors of thromboxane A2 synthase and cAMP phosphodiesterase
AUTHOR(S): Martinez, Gregory R.; Walker, Keith A. M.; Hirschfeld, Donald R.; Bruno, John J.; Yang, Diana S.; Maloney, Patrick J.
CORPORATE SOURCE: Inst. Org. Chem., Syntex Res., Palo Alto, CA, 94304, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 620-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:106055
ED Entered STN: 20 Mar 1992
GI



AB A series of 1H-imidazol-1-yl- and 3-pyridiyl-substituted 3,4-hydroxyquinolin-2(1H)-ones e.g., I (R = 1H-imidazol-1-yl, 3-pyridyl, X = (un)substituted alkylene or unsatd. alkylene) were prepared as combined inhibitors of thromboxanes (TXA2) synthase and cAMP phosphodiesterase (PDE) in human blood platelets. A number of compds. were superior to dazoxiben as inhibitors of TXA2 synthase in vitro ADP-induced aggregation expts. with human blood platelets. The TXA2 synthase inhibitory activity was confirmed by measurement of the prostanoid metabolites derived from 14C-labeled arachidonic acid. Three compds. demonstrated in vitro inhibition of human platelet cAMP PDE at micromolar concns. in conjunction with their TXA2 synthase inhibitory activity. Synergistic enhancement of antiaggregatory and antithrombotic actions was expected when simultaneous stimulation of adenylate cyclase (through increased PGI2 production) and inhibition of platelet cAMP PDE were possible from the same compound I (R = 1H-imidazol-1-yl, X = CH:CH), which has a comparable level of TXA2 synthase (IC50 1.2 μM) and human platelet cAMP PDE (IC50 6.4 μM) inhibitory activities, was found to be orally bioavailable with a long duration of action and offered effective protection against mortality in a collagen-epinephrine-induced pulmonary thromboembolism model in mice. Significant blood pressure and heart rate effects were observed for several compds.

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

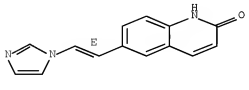
IT 99471-41-7P 119924-94-6P 120067-40-5P 120067-51-8P 120067-52-9P
120067-68-7P 120067-76-7P 120067-77-8P 120067-79-0P 120067-80-3P
120067-81-4P 120067-82-5P 120115-82-4P 138260-79-4P 138260-80-7P
138260-81-8P 138260-82-9P 138260-83-0P 138260-84-1P 138260-85-2P
138260-86-3P 138260-87-4P 138260-88-5P 138260-89-6P 138260-90-9P
138260-92-1P 138260-93-2P 138260-94-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as inhibitor for blood platelet aggregation)

IT 138260-94-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as inhibitor for blood platelet aggregation)

RN 138260-94-3 HCAPLUS

CN 2(1H)-Quinolinone, 6-[2-(1H-imidazol-1-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L88 ANSWER 25 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:583950 HCAPLUS Full-text
DOCUMENT NUMBER: 115:183950

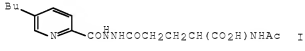
ORIGINAL REFERENCE NO.: 115:31445a,31448a
TITLE: Preparation of amino acid conjugates as renal-selective prodrugs for the treatment of hypertension
INVENTOR(S): Reitz, David B.; Koepke, John P.; Blaine, Edward H.; Schuh, Joseph R.; Manning, Robert E.; Smits, Glenn J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 459 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9101724	A1	19910221	WO 1990-US4168	19900725
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
EP 484437	A1	19920513	EP 1990-912307	19900725
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04506967	T	19921203	JP 1990-511397	19900725
WO 9201667	A1	19920206	WO 1991-US611	19910128
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 20030220521	A1	20031127	US 2002-151211	20020520
US 20040101523	A1	20040527	US 2003-689919	20031020

PRIORITY APPLN. INFO.:

US 1989-386527	A2	19890727
WO 1990-US4168	W	19900725
US 1994-280170	B1	19940725
US 1996-639493	B1	19960429
US 1999-444888	B1	19991122
US 2000-678015	A1	20001002
US 2002-151211	B1	20020520

OTHER SOURCE(S): MARPAT 115:183950
ED Entered STN: 01 Nov 1991
GI



I

AB Title compds., conjugates comprising a 1st residue and a 2nd residue connected by a cleavable bond, wherein the 1st residue is an inhibitor of the biosynthesis of an adrenergic neurotransmitter and the 2nd residue is cleaved by an enzyme located predominantly in the kidney, are prepared 5-[(5-Butyl-2-pyridinyl)carbonyl]-L-glutamic acid hydrazide (preparation given) in MeCN/H2O was treated with 2 equiv of 1M K2CO3 followed by Ac2O and K2CO3 to give the L-glutamic hydrazide I. In spontaneously hypertensive rats, I at 8 mg/h lowered blood pressure from 146 to 122 mm Hg on day 1 and to 115 mm Hg on day 5. Addnl. compds. were prepared and tested. A large number of compds. are claimed.

IC ICM A61K031-12
ICS A61K031-13; A61K031-16; A61K031-33; A61K031-34; A61K031-35; A61K031-38; A61K031-40; A61K031-41; A61K031-46; A61K031-47;

A61K031-50; A61K031-55; A61K031-395; A61K031-405; A61K031-415; A61K031-495; A61K031-535; C07C071-00; C07C211-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63

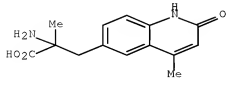
IT 63-91-2DP, L-Phenylalanine, kidney enzyme-cleavable conjugate 66-02-4DP, kidney enzyme-cleavable conjugate 70-78-0DP, kidney enzyme-cleavable conjugate 98-98-6DP, 2-Pyridinecarboxylic acid, kidney enzyme-cleavable conjugate 100-26-5DP, 2,5-Pyridinedicarboxylic acid, kidney enzyme-cleavable conjugate 154-07-4DP, kidney enzyme-cleavable conjugate 300-39-0DP, kidney enzyme-cleavable conjugate 302-53-4DP, kidney enzyme-cleavable conjugate 322-35-0DP, kidney enzyme-cleavable conjugate 331-39-5DP, kidney enzyme-cleavable conjugate 536-69-6DP, kidney enzyme-cleavable conjugate 551-53-1DP, kidney enzyme-cleavable conjugate 555-30-6DP, kidney enzyme-cleavable conjugate 555-62-4DP, kidney enzyme-cleavable conjugate 658-48-0DP, kidney enzyme-cleavable conjugate 672-87-7DP, kidney enzyme-cleavable conjugate 770-08-1DP, kidney enzyme-cleavable conjugate 779-96-4DP, kidney enzyme-cleavable conjugate 831-74-3DP, kidney enzyme-cleavable conjugate 951-55-3DP, kidney enzyme-cleavable conjugate 1081-22-7DP, kidney enzyme-cleavable conjugate 1132-26-9DP, kidney enzyme-cleavable conjugate 1188-37-0DP, kidney enzyme-cleavable conjugate 1784-38-9DP, kidney enzyme-cleavable conjugate 1784-38-9DP, kidney enzyme-cleavable conjugate 3614-72-0DP, kidney enzyme-cleavable conjugate 4298-18-4DP, kidney enzyme-cleavable conjugate 4350-09-8DP, kidney enzyme-cleavable conjugate 4616-70-0DP, kidney enzyme-cleavable conjugate 6548-09-0DP, kidney enzyme-cleavable conjugate 6739-31-7DP, kidney enzyme-cleavable conjugate 7423-93-0DP, kidney enzyme-cleavable conjugate 15069-92-8DP, kidney enzyme-cleavable conjugate 15641-49-3DP, kidney enzyme-cleavable conjugate 16170-76-6DP, kidney enzyme-cleavable conjugate 16709-25-4DP, kidney enzyme-cleavable conjugate 16855-36-0DP, kidney enzyme-cleavable conjugate 16855-37-1DP, kidney enzyme-cleavable conjugate 17243-39-9DP, kidney enzyme-cleavable conjugate 18776-66-4DP, kidney enzyme-cleavable conjugate 18776-68-6DP, kidney enzyme-cleavable conjugate 18776-70-0DP, kidney enzyme-cleavable conjugate 18776-71-1DP, kidney enzyme-cleavable conjugate 18790-58-4DP, kidney enzyme-cleavable conjugate 18790-60-8DP, kidney enzyme-cleavable conjugate 20846-38-2DP, kidney enzyme-cleavable conjugate 20846-40-6DP, kidney enzyme-cleavable conjugate 22818-40-2DP, kidney enzyme-cleavable conjugate 23028-17-3DP, kidney enzyme-cleavable conjugate 23239-35-2DP, kidney enzyme-cleavable conjugate 23365-24-4DP, kidney enzyme-cleavable conjugate 23365-25-5DP, kidney enzyme-cleavable conjugate 23365-26-6DP, kidney enzyme-cleavable conjugate 23365-27-7DP, kidney enzyme-cleavable conjugate 23365-28-8DP, kidney enzyme-cleavable conjugate 23365-30-2DP, kidney enzyme-cleavable conjugate 23365-32-4DP, kidney enzyme-cleavable conjugate 23365-33-5DP, kidney enzyme-cleavable conjugate 23365-34-6DP, kidney enzyme-cleavable conjugate 23365-35-7DP, kidney enzyme-cleavable conjugate 23413-10-7DP, kidney enzyme-cleavable conjugate 24242-20-4DP, kidney enzyme-cleavable conjugate 24593-48-4DP, kidney enzyme-cleavable conjugate 26531-82-8DP, kidney enzyme-cleavable conjugate 28144-67-4DP, kidney enzyme-cleavable conjugate 28484-37-9DP, kidney enzyme-cleavable conjugate 29082-92-6DP, kidney enzyme-cleavable conjugate 30651-24-2DP, kidney enzyme-cleavable conjugate 30766-11-1DP, kidney enzyme-cleavable conjugate 32046-43-8DP, kidney enzyme-cleavable conjugate 32462-30-9DP, kidney enzyme-cleavable conjugate 35115-72-1DP, kidney enzyme-cleavable conjugate 38273-00-6DP, kidney enzyme-cleavable conjugate 42334-89-4DP, kidney enzyme-cleavable conjugate 51814-32-5DP, kidney enzyme-cleavable conjugate 53234-55-2DP, kidney enzyme-cleavable conjugate 53958-19-3DP, kidney enzyme-cleavable

conjugate 62434-97-3DP, kidney enzyme-cleavable conjugate 62435-10-3DP, kidney enzyme-cleavable conjugate 62435-11-4DP, kidney enzyme-cleavable conjugate 62435-13-6DP, kidney enzyme-cleavable conjugate 62435-14-7DP, kidney enzyme-cleavable conjugate 62435-20-5DP, kidney enzyme-cleavable conjugate 62435-21-6DP, kidney enzyme-cleavable conjugate 62435-22-7DP, kidney enzyme-cleavable conjugate 62724-83-8DP, kidney enzyme-cleavable conjugate 64618-91-3DP, kidney enzyme-cleavable conjugate 64618-93-5DP, kidney enzyme-cleavable conjugate 64618-96-8DP, kidney enzyme-cleavable conjugate 64619-01-8DP, kidney enzyme-cleavable conjugate 64619-03-0DP, kidney enzyme-cleavable conjugate 64619-14-3DP, kidney enzyme-cleavable conjugate 64619-20-1DP, kidney enzyme-cleavable conjugate 64619-22-3DP, kidney enzyme-cleavable conjugate1111 64619-24-5DP, kidney enzyme-cleavable conjugate 64619-25-6DP, kidney enzyme-cleavable conjugate 64619-27-8DP, kidney enzyme-cleavable conjugate 64619-32-5DP, kidney enzyme-cleavable conjugate 64619-33-6DP, kidney enzyme-cleavable conjugate 64619-41-6DP, kidney enzyme-cleavable conjugate 64619-42-7DP, kidney enzyme-cleavable conjugate 64619-44-9DP, kidney enzyme-cleavable conjugate 64619-48-3DP, kidney enzyme-cleavable conjugate 64838-54-6DP, kidney enzyme-cleavable conjugate 64991-89-5DP, kidney enzyme-cleavable conjugate 65022-52-8DP, kidney enzyme-cleavable conjugate 66933-04-8DP, kidney enzyme-cleavable conjugate 67605-54-3DP, kidney enzyme-cleavable conjugate 67605-59-8DP, kidney enzyme-cleavable conjugate 67883-95-8DP, kidney enzyme-cleavable conjugate 67883-96-9DP, kidney enzyme-cleavable conjugate 67883-97-0DP, kidney enzyme-cleavable conjugate 67907-09-9DP, kidney enzyme-cleavable conjugate 68351-59-7DP, kidney enzyme-cleavable conjugate 68351-60-0DP, kidney enzyme-cleavable conjugate 69339-97-5DP, kidney enzyme-cleavable conjugate 69356-14-5DP, kidney enzyme-cleavable conjugate 69938-07-4DP, kidney enzyme-cleavable conjugate 69955-03-9DP, kidney enzyme-cleavable conjugate 69955-23-3DP, kidney enzyme-cleavable conjugate 72137-71-4DP, kidney enzyme-cleavable conjugate 72746-40-8DP, kidney enzyme-cleavable conjugate 73088-06-9DP, kidney enzyme-cleavable conjugate 75143-57-6DP, kidney enzyme-cleavable conjugate 75143-58-7DP, kidney enzyme-cleavable conjugate 75143-59-8DP, kidney enzyme-cleavable conjugate 75143-60-1DP, kidney enzyme-cleavable conjugate 75143-60-1P 75143-61-2DP, kidney enzyme-cleavable conjugate 75143-62-3DP, kidney enzyme-cleavable conjugate 75903-35-4DP, kidney enzyme-cleavable conjugate 78168-74-8DP, kidney enzyme-cleavable conjugate 83889-26-3DP, kidney enzyme-cleavable conjugate 83889-28-5DP, kidney enzyme-cleavable conjugate 86873-60-1DP, kidney enzyme-cleavable conjugate 86873-61-2DP, kidney enzyme-cleavable conjugate 86873-62-3DP, kidney enzyme-cleavable conjugate111 86873-64-5DP, kidney enzyme-cleavable conjugate 86873-66-7DP, kidney enzyme-cleavable conjugate 86873-67-8DP, kidney enzyme-cleavable conjugate 88910-31-0DP, kidney enzyme-cleavable conjugate 91248-25-8DP, kidney enzyme-cleavable conjugate 99605-71-7DP, kidney enzyme-cleavable conjugate 99605-73-9DP, kidney enzyme-cleavable conjugate 99605-74-0DP, kidney enzyme-cleavable conjugate 99605-75-1DP, kidney enzyme-cleavable conjugate 99605-76-2DP, kidney enzyme-cleavable conjugate 111462-90-9DP, kidney enzyme-cleavable conjugate 111656-37-2DP, kidney enzyme-cleavable conjugate 113036-59-2DP, kidney enzyme-cleavable conjugate 113036-60-5DP, kidney enzyme-cleavable conjugate 113036-61-6DP, kidney enzyme-cleavable conjugate 113036-63-8DP, kidney enzyme-cleavable conjugate 113036-64-9DP, kidney enzyme-cleavable conjugate 136485-06-8P 136485-07-9P 136485-08-0P 136485-09-1P 136485-10-4P 136485-11-5P 136485-12-6P 136485-13-7DP, kidney enzyme-cleavable conjugate

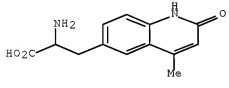
136485-13-7P 136485-14-8P 136485-15-9P 136485-16-0P 136485-17-1DP, kidney enzyme-cleavable conjugate 136485-18-2DP, kidney enzyme-cleavable conjugate 136485-19-3DP, kidney enzyme-cleavable conjugate 136485-21-7DP, kidney enzyme-cleavable conjugate 136485-22-8DP, kidney enzyme-cleavable conjugate 136485-23-9DP, kidney enzyme-cleavable conjugate 136485-24-0DP, kidney enzyme-cleavable conjugate 136485-25-1DP, kidney enzyme-cleavable conjugate 136485-26-2DP, kidney enzyme-cleavable conjugate 136485-27-3DP, kidney enzyme-cleavable conjugate 136485-29-5DP, kidney enzyme-cleavable conjugate 136485-31-9DP, kidney enzyme-cleavable conjugate 136485-34-2DP, kidney enzyme-cleavable conjugate 136485-37-5DP, kidney enzyme-cleavable conjugate 136485-38-6DP, kidney enzyme-cleavable conjugate 136485-39-7DP, kidney enzyme-cleavable conjugate 136485-40-0DP, kidney enzyme-cleavable conjugate 136485-41-1DP, kidney enzyme-cleavable conjugate 136485-44-4DP, kidney enzyme-cleavable conjugate 136485-45-5DP, kidney enzyme-cleavable conjugate 136485-46-6DP, kidney enzyme-cleavable conjugate 136485-47-7DP, kidney enzyme-cleavable conjugate 136485-48-8DP, kidney enzyme-cleavable conjugate 136485-49-9DP, kidney enzyme-cleavable conjugate 136485-50-2DP, kidney enzyme-cleavable conjugate 136485-51-3DP, kidney enzyme-cleavable conjugate 136485-52-4DP, kidney enzyme-cleavable conjugate 136485-53-5DP, kidney enzyme-cleavable conjugate 136485-54-6DP, kidney enzyme-cleavable conjugate 136485-55-7DP, kidney enzyme-cleavable conjugate 136485-56-8DP, kidney enzyme-cleavable conjugate 136485-57-9DP, kidney enzyme-cleavable conjugate 136485-58-0DP, kidney enzyme-cleavable conjugate 136485-59-1DP, kidney enzyme-cleavable conjugate 136485-60-4DP, kidney enzyme-cleavable conjugate 136485-61-5DP, kidney enzyme-cleavable conjugate 136485-62-6DP, kidney enzyme-cleavable conjugate 136485-63-7P 136485-64-8P 136485-65-9P 136485-66-0DP, kidney enzyme-cleavable conjugate 136485-67-1DP, kidney enzyme-cleavable conjugate 136485-68-2DP, kidney enzyme-cleavable conjugate 136485-69-3DP, kidney enzyme-cleavable conjugate 136485-70-6DP, kidney enzyme-cleavable conjugate 136485-71-7DP, kidney enzyme-cleavable conjugate 136485-72-8DP, kidney enzyme-cleavable conjugate 136485-73-9DP, kidney enzyme-cleavable conjugate 136485-74-0DP, kidney enzyme-cleavable conjugate 136485-75-1DP, kidney enzyme-cleavable conjugate 136485-76-2DP, kidney enzyme-cleavable conjugate 136485-77-3DP, kidney enzyme-cleavable conjugate 136485-78-4DP, kidney enzyme-cleavable conjugate 136485-79-5DP, kidney enzyme-cleavable conjugate 136485-80-8DP, kidney enzyme-cleavable conjugate 136485-81-9DP, kidney enzyme-cleavable conjugate 136485-82-0DP, kidney enzyme-cleavable conjugate 136485-83-1DP, kidney enzyme-cleavable conjugate 136485-84-2DP, kidney enzyme-cleavable conjugate 136485-85-3DP, kidney enzyme-cleavable conjugate 136485-86-4DP, kidney enzyme-cleavable conjugate 136485-87-5DP, kidney enzyme-cleavable conjugate 136485-88-6DP, kidney enzyme-cleavable conjugate1111 136485-89-7DP, kidney enzyme-cleavable conjugate 136485-90-0DP, kidney enzyme-cleavable conjugate 136485-91-1DP, kidney enzyme-cleavable conjugate 136485-92-2DP, kidney enzyme-cleavable conjugate 136485-93-3DP, kidney enzyme-cleavable conjugate 136485-94-4DP, kidney enzyme-cleavable conjugate 136485-95-5DP, kidney enzyme-cleavable conjugate 136485-96-6DP, kidney enzyme-cleavable conjugate 136485-97-7DP, kidney enzyme-cleavable conjugate
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as prodrug antihypertensive)

IT 64619-24-5DP, kidney enzyme-cleavable conjugate
64619-25-6DP, kidney enzyme-cleavable conjugate
64619-27-8DP, kidney enzyme-cleavable conjugate
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as prodrug antihypertensive)

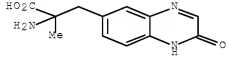
RN 64619-24-5 HCAPLUS
CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-α,4-dimethyl-2-oxo- (CA INDEX NAME)



RN 64619-25-6 HCAPLUS
CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



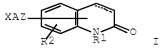
RN 64619-27-8 HCAPLUS
CN 6-Quinoxalinepropanoic acid, α-amino-1,2-dihydro-α-methyl-2-oxo- (CA INDEX NAME)



L88 ANSWER 26 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:128974 HCAPLUS Full-text
DOCUMENT NUMBER: 116:128974
ORIGINAL REFERENCE NO.: 116:21843a,21846a
TITLE: Preparation of (1,2,4-triazol-1-yl)-substituted carbostyril derivatives as platelet aggregation inhibitors
INVENTOR(S): Kano, Masanobu; Tafusa, Fujio; Namikawa, Junichi; Manabe, Yoshiaki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03240786	A	19911028	JP 1990-39518	19900219

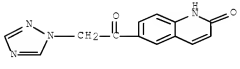
PRIORITY APPLN. INFO.: JP 1990-39518 19900219
OTHER SOURCE(S): CASREACT 116:128974; MARPAT 116:128974
ED Entered STN: 03 Apr 1992
GI



I

AB The title derivs. I [X = 1,2,4-triazol-1-yl; R1 = H, lower alkyl, phenylalkyl; R2 = H, halo, lower alkylsulfonyloxy, lower alkoxy, OH; Z = O, S, CO, C(:NOH), CH(OR3), NH; R3 = H, lower alkyl; A = lower alkylene] and their salts, useful as platelet aggregation inhibitors (no data), are prepared by treating I (X = halo, lower alkylsulfonyloxy, arylsulfonyloxy, aralkylsulfonyloxy) or their salts with 4-amino-1,2,4-triazole (II). A suspension of 7-(3-chloro-1-propoxy)-2(1H)-quinolinone in H2O-DMF mixture was treated with II and NaI under reflux for 11 h to give 66% 7-[3-(1,2,4-triazol-1-yl)propoxy]-3,4-dihydrocarbostyril.

IC ICM C07D401-12
ICS C07D401-06
ICA A61K031-47
CC 28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 70758-97-3P 113855-74-6P 113856-45-4P 113856-70-5P 113856-73-8P
113856-74-9P 113856-80-7P 113857-03-7P 113857-14-0P
113857-15-1P 113857-22-0P 113857-24-2P 113857-30-0P 113857-32-2P
113857-33-3P 113857-37-7P 113857-39-9P 139475-18-6P 139475-19-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as platelet aggregation inhibitor)
IT 113856-80-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as platelet aggregation inhibitor)
RN 113856-80-7 HCAPLUS
CN 2(1H)-Quinolinone, 6-[2-(1H-1,2,4-triazol-1-yl)acetyl]- (CA INDEX NAME)



L88 ANSWER 27 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:514416 HCAPLUS Full-text
DOCUMENT NUMBER: 115:114416
ORIGINAL REFERENCE NO.: 115:19621a,19624a

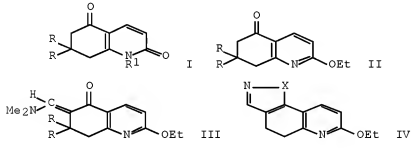
TITLE: Acetals of lactams and acid amides. 60. N- and O-alkylation of some derivatives of 5-oxo-5,6,7,8-tetrahydrocarbostyryl. Syntheses of isoxazolo[5,4-f]- and pyrazolo[3,4-f]quinolines

AUTHOR(S): Shanazarov, A. K.; Kuzovkin, V. A.; Chistyakov, V. V.; Granik, V. G.

CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst., Moscow, 119815, USSR

SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1991), (1), 86-92
CODEN: KGSSAQ; ISSN: 0453-8234

DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 115:114416
ED Entered STN: 23 Sep 1991
GI



AB The alkylation of quinolinone derivs. I (R = Me, H) gives, regardless of reaction conditions and the alkylating agent used [MeNCH(OEt)2, EtI, Et3O+BF4-] the products of N- and O-oxidation If EtI is used, the N-alkylation products, e.g., I (R1 = Et) predominate, while with MeNCH(OEt)2 and Et3O+BF4- the products of O-alkylation, e.g., II become predominant. Further reaction of I (R1 = Et) and II with MeNCH(OEt)2 gives (dimethylamino)methylene derivs., e.g., III. The treatment of the latter derivs. with NH2NH2 or NH2OH gives isoxazolo- or imidazoloquinolines IV (X = O, NH), resp.

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 27

IT 135219-92-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and heterocyclization of, with hydrazine)

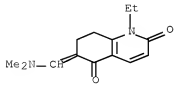
IT 135219-89-5P 135219-91-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

IT 127040-31-7P 135219-87-3P 135219-88-4P 135219-93-1P
135219-94-2P 135219-95-3P 135219-96-4P 135219-97-5P 135219-98-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

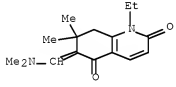
IT 135219-92-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and heterocyclization of, with hydrazine)

RN 135219-92-0 HCAPLUS

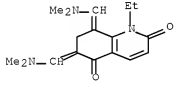
CN 2,5(1H,6H)-Quinolinedione, 6-[(dimethylamino)methylene]-1-ethyl-7,8-dihydro- (CA INDEX NAME)



IT 135219-91-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 135219-91-9 HCAPLUS
CN 2,5(1H,6H)-Quinolinedione, 6-[(dimethylamino)methylene]-1-ethyl-7,8-dihydro-7,7-dimethyl- (CA INDEX NAME)



IT 135219-93-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 135219-93-1 HCAPLUS
CN 2,5(1H,6H)-Quinolinedione, 6,8-bis[(dimethylamino)methylene]-1-ethyl-7,8-dihydro- (CA INDEX NAME)



L88 ANSWER 28 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:228757 HCAPLUS Full-text
DOCUMENT NUMBER: 114:228757
ORIGINAL REFERENCE NO.: 114:38581a,38584a
TITLE: Preparation of (heterocyclylmethoxyphenyl)tetrahydropyrans and related compounds as lipoxygenase inhibitors

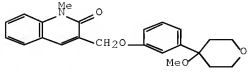
INVENTOR(S): Crawley, Graham Charles; Edwards, Philip Neil; Girodeau, Jean Marc Marie Maurice
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK; ICI-Pharma S. A.
SOURCE: Eur. Pat. Appl., 51 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 385662	A2	19900905	EP 1990-301934	19900222
EP 385662	A3	19911121		
EP 385662	B1	19951213		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9000997	A	19901031	ZA 1990-997	19900209
IL 93342	A	19940530	IL 1990-93342	19900211
CA 2009902	A1	19900831	CA 1990-2009902	19900213
CA 2009902	C	19991005		
AU 9049766	A	19900906	AU 1990-49766	19900214
AU 627275	B2	19920820		
HU 58083	A2	19920128	HU 1990-826	19900216
HU 210165	B	19950228		
AT 131477	T	19951215	AT 1990-301934	19900222
DD 297409	A5	19920109	DD 1990-338111	19900223
NO 175591	B	19940725	NO 1990-916	19900227
NO 175591	C	19941102		
RU 2058306	C1	19960420	RU 1990-4743295	19900227
JP 02268157	A	19901101	JP 1990-46011	19900228
JP 2545629	B2	19961023		
CN 1046903	A	19901114	CN 1990-101081	19900228
CN 1031266	C	19960313		
FI 96512	B	19960329	FI 1990-1008	19900228
KR 195585	B1	19990901	KR 1990-2871	19900228
US 5134148	A	19920728	US 1991-758491	19910905
US 5236919	A	19930817	US 1992-881133	19920511
US 5401751	A	19950328	US 1993-64979	19930524
LT 3396	B	19950925	LT 1993-587	19930531

PRIORITY APPLN. INFO.:

EP 1989-400560	A	19890228
EP 1989-401493	A	19890531
US 1990-485875	B1	19900227
US 1991-758491	A3	19910905
US 1992-881133	A3	19920511

OTHER SOURCE(S): MARPAT 114:228757
ED Entered STN: 15 Jun 1991
GI



I

AB Title compds. QAXArC(OR1)R2R3 [Q = 6-membered monocyclyl or 10-membered bicyclyl containing 1 or 2 N which may bear 2-3 substituents; A = C1-6 alkenylene, C3-5 alkylene, C3-6 alkynylene, cyclo-C3-6-alkylene; X = O, S, SO, SO2, NH; Ar = (substituted) phenylene, 6-membered heterocyclyl containing ≤3 N which may be substituted; R1 = H, C1-6 alkyl, C3-6 alkenyl, C3-6 alkynyl, etc.; R2R3 = (substituted) 4-7-membered ring containing X] 5-lipoxygenase inhibitors useful in treating leukotriene mediated disease, are prepared 3-(Bromomethyl)-1,2-dihydro-1-methylquinolin-2-one (preparation given), 4-(3-hydroxyphenyl)-4-methoxytetrahydropyran (preparation given), K2CO3 and DMF were stirred at ambient temperature for 15 h to give pyran I. Title compds. inhibited 5-LO with IC50's of 0.01-30 micromolar. Pharmaceutical formulations comprising the title compds. are given.

IC ICM C07D405-12
ICS C07D405-14; A61K031-47; A61K031-44; A61K031-495

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63

IT 133739-00-1P 133739-01-2P 133739-02-3P 133739-03-4P 133739-04-5P
133739-05-6P 133739-06-7P 133739-07-8P 133739-08-9P 133739-09-0P
133739-10-3P 133739-11-4P 133739-12-5P 133739-13-6P 133739-14-7P
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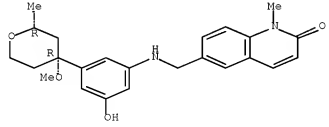
133739-50-1P 133739-51-2P 133739-52-3P 133739-53-4P 133739-54-5P
133739-55-6P 133739-56-7P 133739-57-8P 133739-58-9P
133739-59-0P 133759-47-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-lipoxygenase inhibitor)

IT 133739-55-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-lipoxygenase inhibitor)

RN 133739-55-6 HCAPLUS

CN 2(1H)-Quinolinone, 6-[[[3-hydroxy-5-[(2R,4R)-tetrahydro-4-methoxy-2-methyl-2H-pyran-4-yl]phenyl]amino]methyl]-1-methyl-, rel- (CA INDEX NAME)

Relative stereochemistry.



L88 ANSWER 29 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:407401 HCAPLUS Full-text
DOCUMENT NUMBER: 111:7401
ORIGINAL REFERENCE NO.: 111:1422h,1423a
TITLE: Imidazole- or pyridine-containing carbostyrils as combined thromboxane synthetase and cyclic-AMP

phosphodiesterase inhibitors, their preparation, and pharmaceuticals containing them

INVENTOR(S): Walker, Keith A. M.; Bruno, John J.; Martinez, Gregory R.

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA

SOURCE: U.S., 20 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

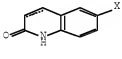
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4792561	A	19881220	US 1986-868845	19860529
US 4921862	A	19900501	US 1988-247134	19880921

PRIORITY APPLN. INFO.: US 1986-868845 A3 19860529

OTHER SOURCE(S): CASREACT 111:7401; MARPAT 111:7401

ED Entered STN: 08 Jul 1989

GI



I

AB Title compds. I [X = R1CR2, cis- or trans-CR3:CR4; R1 = H when R2 = OH, or R1 = Ph, phenylalkyl when R2 = H, OH; Ph is optionally monosubstituted; or R1R2 = O, C1-6 alkylidene, (substituted) benzylidene; R3 = H, C1-6 alkyl; R4 = H; R3R4 = bond; n = 0-3; R = 1-imidazolyl; dotted line = optional covalent bond] are prepared as thromboxane synthetase and cAMP phosphodiesterase inhibitors for treatment of disease characterized by elevated thromboxane levels or an imbalance of prostacyclin/thromboxane levels (no data). A mixture of CuI 11.6, (Ph3P)2PdCl2 86, N-propargylimidazole (preparation given) 774 mg, and 6-bromo-3,4-dihydrocarbostyril 1.5 g was stirred in 10mL pyridine and 2 mL triethylamine at 100° for 48 h under N. The reaction mixture was then treated with saturated aqueous K2CO3, extracted with 10% MeOH in CH2Cl2, and worked up to give 6-[3-(imidazol-1-yl)-1-propyn-1-yl]-3,4- dihydrocarbostyril. The latter (502 mg) was stirred under H in the presence of 200 mg 10% Pd/C to give 6-[3-(imidazol-1-yl)propyl]-3,4-dihydrocarbostyril (II). A tablet was formulated containing II 25, cornstarch 20, spray-dried lactose 153, and Mg stearate 2 mg.

IC ICM C07D401-06
ICS C07D401-10; C07D401-12; A61K031-47

INCL 514312000

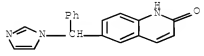
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7, 27, 63

IT 119924-94-6P 120067-40-5P 120067-41-6P 120067-42-7P
120067-43-8P 120067-44-9P 120067-45-0P 120067-51-8P
120067-52-9P 120067-53-0P 120067-54-1P 120067-56-3P,
6-(3-Pyridylacetyl)-3,4-dihydrocarbostyril 120067-57-4P 120067-58-5P
120067-59-6P 120067-60-9P 120067-61-0P 120067-62-1P 120067-63-2P
120067-64-3P 120067-65-4P 120067-66-5P 120067-68-7P 120067-69-8P
120067-70-1P 120067-71-2P 120067-72-3P 120067-73-4P 120067-74-5P
120067-75-6P 120067-76-7P 120067-77-8P 120067-78-9P 120067-79-0P
120067-80-3P 120067-81-4P 120067-82-5P

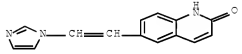
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cAMP phosphodiesterase and thromboxane synthetase inhibitors)

IT 120067-41-6P 120067-44-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cAMP phosphodiesterase and thromboxane synthetase inhibitors)

RN 120067-41-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-(1H-imidazol-1-ylphenylmethyl)- (CA INDEX NAME)



RN 120067-44-9 HCAPLUS
CN 2(1H)-Quinolinone, 6-[2-(1H-imidazol-1-yl)ethenyl]- (CA INDEX NAME)

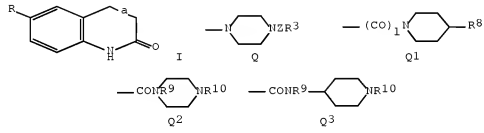


L88 ANSWER 30 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:422851 HCAPLUS Full-text
DOCUMENT NUMBER: 109:22851
ORIGINAL REFERENCE NO.: 109:3905a,3908a
TITLE: Preparation of carbostyril derivatives, compositions containing them, and their use as cardiotonics
INVENTOR(S): Tamada, Shigeharu; Fujioka, Takafumi; Ogawa, Hidenori; Teramoto, Shuji; Kondo, Kazumi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 112 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 255134	A2	19880203	EP 1987-111045	19870730
EP 255134	A3	19900523		
EP 255134	B1	19930303		
R: CH, DE, ES, FR, GB, IT, LI, NL, SE				
JP 63035562	A	19880216	JP 1986-181662	19860731
JP 06096555	B	19941130		
JP 64003182	A	19890106	JP 1987-156887	19870624
JP 07045493	B	19950517		
DK 8703973	A	19880201	DK 1987-3973	19870730

US 4886809	A	19891212	US 1987-79875		19870730
ES 2053480	T3	19940801	ES 1987-111045		19870730
US 5071856	A	19911210	US 1989-405295		19890911
US 5306719	A	19940426	US 1991-760480		19910916
PRIORITY APPLN. INFO.:			JP 1986-181662	A	19860731
			JP 1987-156887	A	19870624
			US 1987-79875	A3	19870730
			US 1989-405295	A3	19890911

OTHER SOURCE(S): CASREACT 109:22851; MARPAT 109:22851
ED Entered STN: 22 Jul 1988
GI



AB The title compds. [I; R = ANR1R2, Q1, Q2; A = CO, C(:NOH)B; B = alkylene; R1, R2 = alkyl, phenylalkyl, alkoxyphenylalkyl; NR1R2 = Q; R3 = (un)substituted Ph; Z = CO, BC:NR4, ACHR5; R4 = OH, alkanoyloxy, alkoxy; R5 = cyano, halo, NR6R7; R6, R7 = H, alkyl, etc.; NR6R7 = heterocyclyl; R8 = alkylenedioxy, oxo, NOH, NR11R12; R9 = H, alkyl; R10 = H, alkyl, alkanoyl, (un)substituted phenylalkyl, etc.; R11, R12 = H, alkyl, etc.; a = single or double bond; l = 0, 1] were prepared 6-Carboxy-3,4-dihydrocarbostyril was stirred with (3-hydroxyimino-3-phenylpropyl)piperazine at 60-70° for 5 h in dioxane containing DCC to give 6-[4-(3-hydroxyimino-3-phenylpropyl)-1- piperazinylcarbonyl]-3,4-dihydrocarbostyril (II) which, administered intraarterially in perfused blood, gave 77% change of dog ventricular muscle contraction in vitro. Tablets were prepared each containing II 5, starch 132, Mg stearate 18, and lactose 45 mg.

IC ICM C07D215-22
ICS C07D215-48; C07D401-12; C07D405-12; C07D401-06; C07D491-10; C07D401-04; A61K031-47

ICA C07C121-66; C07D295-12

ICI C07D491-10, C07D317-00, C07D221-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT

115064-62-5P	115064-63-6P	115064-64-7P	115064-65-8P	115064-67-0P
115064-68-1P	115064-69-2P	115064-70-5P	115064-71-6P	115064-72-7P
115064-73-8P	115064-74-9P	115064-76-1P	115064-78-3P	115064-80-7P
115064-81-8P	115064-82-9P	115064-84-1P	115064-86-3P	115064-88-5P
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115064-98-7P	115065-00-4P	115065-01-5P	115065-02-6P	
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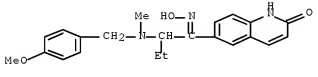
115065-65-1P 115075-84-8P 115090-90-9P 115090-91-0P 115090-92-1P
115090-93-2P 115090-94-3P 115090-95-4P 115090-96-5P 115091-07-1P
115091-16-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiotonic)

IT 115065-03-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiotonic)

RN 115065-03-7 HCAPLUS

CN 2(1H)-Quinolinone, 6-[1-(hydroxyimino)-2-[[(4-methoxyphenyl)methyl]methylamino]butyl]- (CA INDEX NAME)



L88 ANSWER 31 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

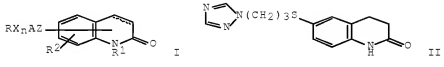
ACCESSION NUMBER:	1988:167318 HCAPLUS Full-text
DOCUMENT NUMBER:	108:167318
ORIGINAL REFERENCE NO.:	108:27501a,27504a
TITLE:	Preparation of heterocyclic carbostyril derivatives as inhibitors of thrombocyte adhesion
INVENTOR(S):	Nishi, Takao; Uno, Tetsuyuki; Koga, Yasuo; Chu, Gil Namg
PATENT ASSIGNEE(S):	Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE:	Eur. Pat. Appl., 204 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 240015	A2	19871007	EP 1987-104873	19870402
EP 240015	A3	19901024		
EP 240015	B1	19941228		
R: CH, DE, ES, FR, GB, IT, LI, NL, SE				
JP 63045220	A	19880226	JP 1987-43457	19870225
JP 06081727	B	19941019		
JP 01006271	A	19890110	JP 1987-60770	19870316
JP 06081752	B	19941019		
DK 8701671	A	19871003	DK 1987-1671	19870401

ES 2068807	T3	19950501	ES 1987-104873		19870402
US 5008274	A	19910416	US 1988-232524		19880816
US 5434164	A	19950718	US 1992-958489		19921008
PRIORITY APPLN. INFO.:			JP 1986-76089	A	19860402
			JP 1987-43457	A	19870225
			JP 1987-60770	A	19870316
			JP 1987-43458	A1	19870225
			US 1987-36564	B1	19870331
			US 1988-232524	A3	19880816
			US 1990-625018	B1	19901210

OTHER SOURCE(S): MARPAT 108:167318
ED Entered STN: 13 May 1988
GI



AB The title compds. [I; A = alkylene; R = (un)substituted, unsatd. heterocyclyl containing 1-4 O, S, N; R1 = H, alkyl, phenylalkyl; R2 = H, alkoxy, alkylsulfonyloxy, OH, halo; X = O, S, SO, SO2; Z = O, S, CO, HON:C, R1OCH, NH; n = 0, 1; dotted line indicates optional carbostyryl double bond] and their salts were prepared as blood platelet aggregation inhibitors. A mixture of 2.4 g 6-mercapto-3,4-dihydrocarbostyril, 3.3 g 1-(3-bromopropyl)-1,2,4-triazole, and 2.6 mL 1,8-diazabicyclo[5.4.0]undec-7-ene was refluxed 2 h in 60 mL Me2CHOH to give 2.5 g [(triazolylpropyl)thio]carbostyril II. In rats 100 mg II/kg orally reduced blood platelet aggregation 57%. Tablets were prepared containing 6-[[(1-phenyl-1H-imidazol-2-yl)thio]acetyl]-3,4-dihydrocarbostyril 5, lactose 50, cornstarch 25, microcryst. cellulose 25, methylcellulose 1.5, and Mg stearate 1.0 g per 103 tablets.

IC ICM C07D401-06
ICS C07D417-06; C07D413-06; C07D409-06; C07D405-06; C07D401-12; C07D417-12; C07D413-12; C07D409-12; C07D405-12; C07D401-14

ICA C07D405-04; C07D405-14; C07C133-02

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63

IT 70758-97-3P 70758-98-4P 81914-13-8P 81914-16-1P 81914-18-3P
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113857-30-0P	113857-31-1P	113857-32-2P	113857-33-3P	113857-34-4P
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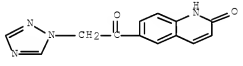
113857-40-2P	113857-41-3P	113857-42-4P	113857-43-5P	113857-44-6P
113857-45-7P	113885-64-6P	113885-65-7P	113885-66-8P	113885-67-9P
113885-68-0P	113885-69-1P	114080-90-9P		

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as blood platelet aggregation inhibitor)

IT 113856-80-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as blood platelet aggregation inhibitor)

RN 113856-80-7 HCAPLUS

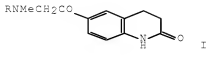
CN 2(1H)-Quinolinone, 6-[2-(1H-1,2,4-triazol-1-yl)acetyl]- (CA INDEX NAME)



L88 ANSWER 32 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1988:131551 HCAPLUS Full-text
DOCUMENT NUMBER:	108:131551
ORIGINAL REFERENCE NO.:	108:21575a,21578a
TITLE:	Studies on positive inotropic agents. III. Synthesis of 6-(substituted 1-oxoalkyl)-2(1H)-quinolinone derivatives
AUTHOR(S):	Tominaga, Michiaki; Ogawa, Hidenori; Yo, Eiyu; Yamashita, Syuji; Yabuuchi, Youichi; Nakagawa, Kazuyuki
CORPORATE SOURCE:	Tokushima Res. Inst., Otsuka Pharm. Co., Ltd., Tokushima, 771-01, Japan
SOURCE:	Yakugaku Zasshi (1987), 107(6), 420-8 CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE:	Journal
LANGUAGE:	Japanese
OTHER SOURCE(S):	CASREACT 108:131551

ED Entered STN: 15 Apr 1988
GI



I

AB Many 3,4-dihydro-6-(substituted 1-oxoalkyl)-2(1H)-quinolinone derivs. were synthesized and examined for pos. inotropic activity on the canine heart. Among them, 3,4-dihydro-6-[2-(N-methyl-4-methoxybenzylamino)acetyl]-2(1H)-quinolinone (I, R = 4-MeOC6H4CH2), 3,4-dihydro-6-[2-(N-methyl-4-cyanobenzylamino)acetyl]-2(1H)-quinolinone (I, R = 4-NCC6H4CH2) and 6-[2-(N-methyl-4-methoxybenzylamino)acetyl]-2(1H)-quinolinone were found to have a potent pos. inotropic activity with little chronotropic effect.

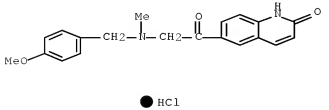
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 61122-77-8P 61122-80-3P 63423-84-7P 80835-16-1P 83734-49-0P
86061-39-4P 86061-40-7P 86061-41-8P 86061-66-7P 86061-70-3P
86092-75-3P 86092-83-3P 86092-88-8P 86092-89-9P 86092-90-2P
86092-94-6P 90775-72-7P 90775-73-8P 90775-74-9P 113470-49-8P
113470-50-1P 113470-51-2P 113470-52-3P 113470-53-4P 113470-54-5P
113470-55-6P 113470-56-7P 113470-57-8P 113470-58-9P 113470-59-0P
113470-60-3P 113470-61-4P 113470-62-5P 113470-63-6P 113470-64-7P
113470-65-8P 113470-66-9P 113470-67-0P 113470-68-1P 113470-69-2P
113470-70-5P 113470-71-6P 113470-72-7P 113470-73-8P 113470-74-9P
113470-75-0P 113470-76-1P 113470-77-2P 113470-78-3P
113489-11-5P 113489-12-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and cardiotonic activity of)

IT 113489-11-5P 113489-12-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and cardiotonic activity of)

RN 113489-11-5 HCAPLUS

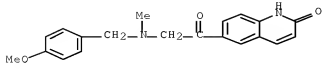
CN 2(1H)-Quinolinone, 6-[2-[[(4-methoxyphenyl)methyl]methylamino]acetyl]-, hydrochloride (1:1) (CA INDEX NAME)



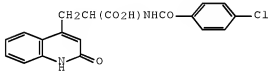
● HCl

RN 113489-12-6 HCAPLUS

CN 2(1H)-Quinolinone, 6-[2-[[(4-methoxyphenyl)methyl]methylamino]acetyl]- (CA INDEX NAME)



L88 ANSWER 33 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:497287 HCAPLUS Full-text
DOCUMENT NUMBER: 105:97287
ORIGINAL REFERENCE NO.: 105:15717a,15720a
TITLE: Studies on 2(1H)-quinolinone derivatives as gastric antiulcer active agents. 2-(4-Chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]propionic acid and related compounds
AUTHOR(S): Uchida, Minoru; Tabusa, Fujio; Komatsu, Makoto; Morita, Seiji; Kanbe, Toshimi; Nakagawa, Kazuyuki
CORPORATE SOURCE: Tokushima Res. Inst., Otsuka Pharm. Co., Ltd., Tokushima, 771-01, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1985), 33(9), 3775-86
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:97287
ED Entered STN: 19 Sep 1986
GI



I

AB N-Acyl amino acid analogs of 2(1H)-quinolinone, e.g., I, were prepared and tested for antiulcer activity in rats. These compds. were prepared by acylation of amino acid derivs. of 2(1H)-quinolinone, which were obtained from the reaction of ω-bromoalkyl-2(1H)-quinolinones and acetamidomalonate in the presence of NaOEt, followed by hydrolysis with dilute HCl. I had the most potent activity.
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 103702-41-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of)
IT 90097-98-6P 90097-99-7P 90098-03-6P 90098-04-7P 90098-05-8P
90098-06-9P 90098-08-1P 90098-09-2P 90098-10-5P 90098-16-1P

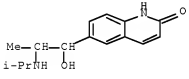
90098-17-2P 90098-24-1P 90098-33-2P 90098-34-3P 90098-38-7P
90098-42-3P 90098-43-4P 90098-47-8P 90098-86-5P 103702-31-4P
103702-37-0P 103702-38-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiulcer activity of)

IT 4900-38-3P 90097-63-5P 90097-71-5P 90097-80-6P 103702-30-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of)

IT 103702-41-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of)

RN 103702-41-6 HCAPLUS

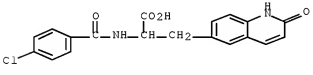
CN 2(1H)-Quinolinone, 6-[1-hydroxy-2-[(1-methylethyl)amino]propyl]- (CA INDEX NAME)



IT 103702-38-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiulcer activity of)

RN 103702-38-1 HCAPLUS

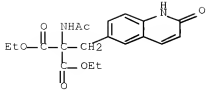
CN 6-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



IT 103702-30-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of)

RN 103702-30-3 HCAPLUS

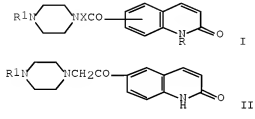
CN Propanedioic acid, 2-(acetylamino)-2-[(1,2-dihydro-2-oxo-6-quinolinyl)methyl]-, 1,3-diethyl ester (CA INDEX NAME)



L88 ANSWER 34 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1983:405649 HCAPLUS Full-text
DOCUMENT NUMBER: 99:5649
ORIGINAL REFERENCE NO.: 99:1033a,1036a
TITLE: Carbostyril derivatives and pharmaceutical compositions containing them
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd. , Japan
SOURCE: Belg., 76 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 894105	A1	19830214	BE 1982-208806	19820813
JP 58038258	A	19830305	JP 1981-137984	19810901
JP 01003194	B	19890119		
JP 58110568	A	19830701	JP 1981-210368	19811225
JP 03010620	B	19910214		
AU 8286980	A	19830414	AU 1982-86980	19820809
AU 532361	B2	19830929		
FI 8202803	A	19830302	FI 1982-2803	19820811
FI 78688	B	19890531		
FI 78688	C	19890911		
ZA 8205818	A	19830629	ZA 1982-5818	19820811
US 4514401	A	19850430	US 1982-407099	19820811
CA 1205807	A1	19860610	CA 1982-409255	19820811
DK 8203619	A	19830302	DK 1982-3619	19820812
DK 166877	B1	19930726		
NO 8202749	A	19830302	NO 1982-2749	19820812
NO 159591	B	19881010		
NO 159591	C	19890118		
SE 8204677	A	19830302	SE 1982-4677	19820813
SE 452984	B	19880104		
SE 452984	C	19880414		
FR 2512019	A1	19830304	FR 1982-14117	19820813
FR 2512019	B1	19860103		
DE 3230209	A1	19830310	DE 1982-3230209	19820813
DE 3230209	C2	19850822		
GB 2108109	A	19830511	GB 1982-23310	19820813
GB 2108109	B	19850509		
SU 1356962	A3	19871130	SU 1982-3485500	19820813
CH 650783	A5	19850815	CH 1982-4880	19820815
AT 8203106	A	19861215	AT 1982-3106	19820816
AT 383592	B	19870727		
NL 8203225	A	19830405	NL 1982-3225	19820817

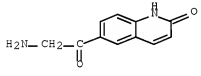
PRIORITY APPLN. INFO.: JP 1981-137984 A 19810901
JP 1981-210368 A 19811225
OTHER SOURCE(S): CASREACT 99:5649; MARPAT 99:5649
ED Entered STN: 12 May 1984
GI



I

II

AB Piperazinoalkanoylcarbostyriles I (R = H, alkyl, aralkyl; R1 = acyl, alkylsulfonyl, arylsulfonyl, phenoxyalkyl; X = alkylene) and their 3,4-dihydro derivs. were prepared Thus, II (R1 = H) was acylated to give II (R1 = 3-ClC6H4CO) which at 1 μmole gave a 60% increase in the contraction of dog papillary muscle in vitro.
ICI A61
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
IT 86061-41-8 86061-54-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bis(hydroxyethyl)amine)
IT 86061-54-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bis(hydroxyethyl)amine)
RN 86061-54-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-(2-aminoacetyl)- (CA INDEX NAME)

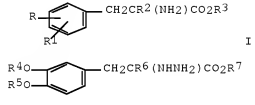


L88 ANSWER 35 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1979:611822 HCAPLUS Full-text
DOCUMENT NUMBER: 91:211822
ORIGINAL REFERENCE NO.: 91:34149a,34152a
TITLE: Antihypertensive compositions containing an aryl-substituted alanine azo and an arylhydrazinopropionic acid
INVENTOR(S): Stone, Clement A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4156734	A	19790529	US 1978-877532	19780213
US 4160835	A	19790710	US 1977-850755	19771111
US 4170654	A	19791009	US 1978-922460	19780706
PRIORITY APPLN. INFO.:			US 1976-657822	A2 19760213
			US 1976-743369	A1 19761119
			US 1977-850755	A3 19771111

OTHER SOURCE(S): MARPAT 91:211822
ED Entered STN: 12 May 1984
GI



AB 3-Arylalanines I (R = H, CO2H, CN, NCNH, CSNH2, H2NCH2CH2, guanidino, OH, MeSO2NH, NO2, NH2, MeSO3, H2OCCH2O, formyl, MeO; R1 = substituted or unsubstituted 5-membered heterocyclic ring containing 1 or more N atoms; R2 and R3 = H, C1-4 alkyl) and decarboxylase-inhibiting α-hydrazinodopa analogs II (R4, R5, R6, and R7 = H, C1-4 alkyl) were prepared as antihypertensives. Thus, 4-amino-α-methyl-DL-phenylalanine dihydrochloride was treated with BrCN in H2O containing NaOAc for 30 min to give a mixture which was treated with more BrCN for 16 h at room temperature to give 77% DL-I (R = R3 = H, R1 = NCNH, R2 = Me) (III). Sixty-nine other examples are given. III at 0.3 mg/kg exhibited a slightly active antihypertensive rating in rats.

IC A61K031-24; A61K031-40; A61K031-195; A61K031-415
INCL 424273000R
CC 34-2 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63
IT 150-30-1DP, derivs. 302-72-7DP, 3-aryl derivs. 64618-91-3P
64618-93-5P 64618-95-7P 64618-96-8P 64618-97-9P 64618-99-1P
64619-01-8P 64619-08-5P 64619-11-0P 64619-15-4P 64619-17-6P
64619-18-7P 64619-21-2P 64619-24-5P 64619-26-7P
64619-29-0P 64619-30-3P 64619-32-5P 64619-33-6P 64619-34-7P
64619-41-6P 64619-43-8P 64619-45-0P 64619-49-4P 64619-57-4P
64619-69-8P 71920-95-1P 71921-10-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antihypertensive activity of)
IT 64619-63-2P 64619-68-7P 64619-73-4P 64619-80-3P 64619-84-7P
64619-85-8P 64619-86-9P 64619-88-1P 64620-01-5P 64620-05-9P
64991-74-8P 64991-83-9P 64992-02-5P 65022-50-6P 65022-51-7P
65091-42-1P 71920-85-9P 71920-90-6P 71920-94-0P 71921-00-1P

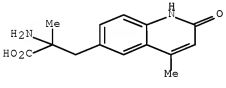
71921-03-4P 71921-04-5P 71921-08-9P 71921-09-0P 71921-12-5P
71921-14-7P 71921-15-8P 71935-08-5P 71935-11-0P
71935-12-1P 71935-15-4P 71935-19-8P 71935-20-1P 71935-25-6P
71935-27-8P 71935-30-3P 71935-34-7P 71935-35-8P 71935-37-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

IT 302-53-4P 28860-95-9P 64618-92-4P 64619-00-7P 64619-02-9P
64619-03-0P 64619-04-1P 64619-05-2P 64619-06-3P 64619-10-9P
64619-12-1P 64619-14-3P 64619-16-5P 64619-19-8P 64619-20-1P
64619-22-3P 64619-25-6P 64619-27-8P 64619-28-9P
64619-31-4P 64619-37-0P 64619-38-1P 64619-40-5P 64619-48-3P
64619-50-7P 64619-51-8P 64619-52-9P 64619-53-0P 64619-54-1P
64619-56-3P 64722-27-6P 64723-08-6P 64723-09-7P 64991-81-7P
64991-89-5P 64991-96-4P 64991-99-7P 65022-52-8P 71920-87-1P
71920-91-7P 71920-98-4P 71920-99-5P 71921-17-0P 71935-07-4P
71935-13-2P 71935-14-3P 71935-39-2P 136523-06-3P 136523-08-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 64619-24-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antihypertensive activity of)

RN 64619-24-5 HCAPLUS

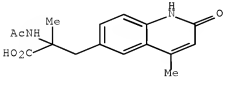
CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-α,4-dimethyl-2-oxo- (CA INDEX NAME)



IT 71921-12-5P 71921-14-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

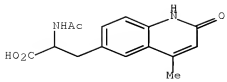
RN 71921-12-5 HCAPLUS

CN 6-Quinolinepropanoic acid, α-(acetylamino)-1,2-dihydro-α,4-dimethyl-2-oxo- (CA INDEX NAME)

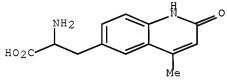


RN 71921-14-7 HCAPLUS

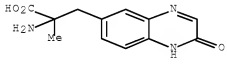
CN 6-Quinolinepropanoic acid, α-(acetylamino)-1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



IT 64619-25-6P 64619-27-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 64619-25-6 HCAPLUS
CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



RN 64619-27-8 HCAPLUS
CN 6-Quinoxalinepropanoic acid, α-amino-1,2-dihydro-α-methyl-2-oxo- (CA INDEX NAME)



L88 ANSWER 36 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1977:577980 HCAPLUS Full-text
DOCUMENT NUMBER: 87:177980
ORIGINAL REFERENCE NO.: 87:28067a,28070a
TITLE: Antihypertonic preparations
INVENTOR(S): Stone, Clement Addison
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2705863	A1	19770818	DE 1977-2705863	19770211

NL 7700945	A	19770816	NL 1977-945		19770128
BE 851051	A1	19770803	BE 1977-174629		19770203
AU 7721920	A	19780810	AU 1977-21920		19770203
AU 511964	B2	19800918			
JP 52099227	A	19770819	JP 1977-13082		19770210
FR 2340729	A1	19770909	FR 1977-3908		19770211
FR 2340729	B1	19790824			
ZA 7700815	A	19780927	ZA 1977-815		19770211
US 4170654	A	19791009	US 1976-657822	A	19760213
			US 1976-743369	A3	19761119
			US 1977-850755	A3	19771111

PRIORITY APPLN. INFO.:

ED Entered STN: 12 May 1984

AB Aryl substituted alanines were prepared and tested with the decarboxylase inhibitor carbidopa [28860-95-9] for antihypertensive activity in spontaneously hypertensive rats. The antihypertensive activity of the alanine compds. was potentiated by addition of the decarboxylase inhibitor. Antihypertensive activity was also observed when nonantihypertensive arylalanines were combined with nonantihypertensive carbidopa. This potentiating effect of carbidopa was observed whether compound administration was oral or parenteral, sep. or simultaneous, or as mixts.

IC A61K031-22

CC 1-5 (Pharmacodynamics)

IT 64618-91-3P 64618-93-5P 64618-95-7P 64618-96-8P 64618-97-9P
64618-98-0P 64618-99-1P 64619-01-8P 64619-02-9P 64619-06-3P
64619-07-4P 64619-08-5P 64619-09-6P 64619-11-0P 64619-15-4P
64619-17-6P 64619-18-7P 64619-21-2P 64619-24-5P
64619-26-7P 64619-29-0P 64619-30-3P 64619-32-5P 64619-33-6P
64619-34-7P 64619-35-8P 64619-41-6P 64619-43-8P 64619-45-0P
64619-49-4P 64619-57-4P 136485-31-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antihypertensive activity of)

IT 15150-25-1P 64611-04-7P 64618-92-4P 64618-94-6P 64619-00-7P
64619-03-0P 64619-04-1P 64619-05-2P 64619-10-9P 64619-12-1P
64619-14-3P 64619-16-5P 64619-19-8P 64619-20-1P 64619-22-3P
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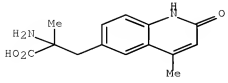
64722-27-6P 64723-07-5P 64723-08-6P 64723-09-7P 73088-06-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 64619-24-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antihypertensive activity of)

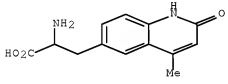
RN 64619-24-5 HCAPLUS

CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-α,4-dimethyl-2-

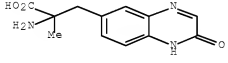
oxo- (CA INDEX NAME)



IT 64619-25-6P 64619-27-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 64619-25-6 HCAPLUS
CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



RN 64619-27-8 HCAPLUS
CN 6-Quinoxalinepropanoic acid, α-amino-1,2-dihydro-α-methyl-2-oxo- (CA INDEX NAME)

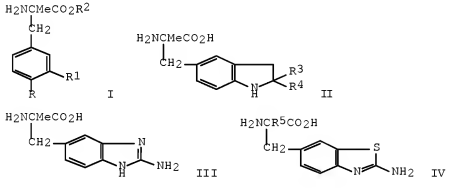


L88 ANSWER 37 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1978:23389 HCAPLUS Full-text
DOCUMENT NUMBER: 88:23389
ORIGINAL REFERENCE NO.: 88:3777a,3780a
TITLE: Substituted alanine derivatives
INVENTOR(S): Atkinson, Joseph George; Rooney, Clarence Stanley; Girard, Yves; Engelhardt, Edward Louis
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Ger. Offen., 65 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 2705816	A1	19770818	DE 1977-2705816		19770211
US 4065572	A	19771227	US 1976-657827		19760213
DK 7700313	A	19770814	DK 1977-313		19770125
NL 7700951	A	19770816	NL 1977-951		19770128
SE 7701505	A	19770814	SE 1977-1505		19770210
JP 52097933	A	19770817	JP 1977-13086		19770210
GB 1554667	A	19791024	GB 1977-5517		19770210
FR 2400008	A1	19790309	FR 1977-3912		19770211
CH 626871	A5	19811215	CH 1977-1727		19770211
US 4153715	A	19790508	US 1977-825013		19770816
US 4206216	A	19800603	US 1978-912593		19780605
US 4271187	A	19810602	US 1979-76650		19790918
PRIORITY APPLN. INFO.:			US 1976-657827	A	19760213
			US 1977-825013	A3	19770816
			US 1978-912593	A3	19780605

OTHER SOURCE(S): CASREACT 88:23389; MARPAT 88:23389
ED Entered STN: 12 May 1984
GI



AB DL-Phenylalanines I (R = NHCN, H, CSNH2, guanidino, NHSO2Me, NH2, NO2, pyrrol-1-yl, imidazol-2-yl, 2-aminoimidazol-1-yl, imidazol-2-ylamino, etc.; R1 = H, CO2H, OH, OSO2Me, CO2Me, NO2, NH2; R2 = H, Me) (14 compds.), heterocyclic DL-alanines II (R3 = R4 = H; R3R4 = O), III, and IV (R5 = H, Me) and .apprx.45 similar DL-alanine derivs. as well as 2 L-alanine and 1 D-alanine derivative were prepared as antihypertensives (many of the derivs. were isolated as HCl or oxalate salts). Thus, MeCH(NCO)CO2Me was treated with BrCH2C6H4CN-p in DMF containing NaOMe to give 80% DL-p-NCC6H4CH2CMe(NCO)CO2Me, which was treated with HCl to give 60% DL-p-NCC6H4CH2CMe(NHCHO)CO2Me. The latter was treated with H2S in pyridine to give 94% DL-p-(H2NCS)C6H4CH2CMe(NHCHO)CO2Me, which was treated with HCl in MeOH to give I (R = CSNH2, R1 = H, R2 = Me). Pharmaceutical formulations are given.

IC C07D247-00

CC 34-2 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63

IT 64618-91-3P 64618-92-4P 64618-93-5P 64618-94-6P 64618-95-7P
64618-96-8P 64618-97-9P 64618-98-0P 64618-99-1P 64619-00-7P
64619-01-8P 64619-02-9P 64619-03-0P 64619-04-1P 64619-05-2P
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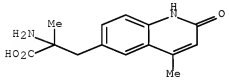
73088-06-9P 136485-21-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 64619-24-5P 64619-25-6P 64619-27-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

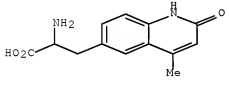
RN 64619-24-5 HCAPLUS

CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-α,4-dimethyl-2-oxo- (CA INDEX NAME)



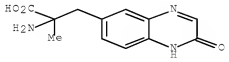
RN 64619-25-6 HCAPLUS

CN 6-Quinolinepropanoic acid, α-amino-1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



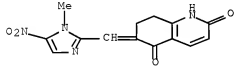
RN 64619-27-8 HCAPLUS

CN 6-Quinoxalinepropanoic acid, α-amino-1,2-dihydro-α-methyl-2-oxo- (CA INDEX NAME)



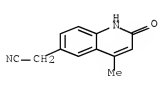
L88 ANSWER 38 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1975:593044 HCAPLUS Full-text
DOCUMENT NUMBER: 83:193044
ORIGINAL REFERENCE NO.: 83:30349a,30352a
TITLE: Chemotherapeutic nitroheterocycles. 17. Condensation products of nitrated heterocyclic aldehydes with oxocyclopentathiophenes and oxotetrahydroquinolines
AUTHOR(S): Albrecht, R.; Schroeder, E.
CORPORATE SOURCE: Forschungslab., Schering A.-G., Berlin, Fed. Rep. Ger.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1975), 308(8), 588-94
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB Sixteen condensation products I (X = O, S, NH, X1 = CH; X = NMe, X1 = N; X2 = CH2, CH2CH2, SCH2; X3 = 1-thiophene, 2-thiophene, dimethyl-2-thiophene, dichloro-2-thiophene, pyridone, methylpyridone, alkoxypyridine moiety) of 5-nitrofurfural, 5-nitro-2-thiophenecarboxaldehyde II, II diacetate, 5-nitropyrrole-2-carboxaldehyde, and 1-methyl-5-nitroimidazole-2-carboxaldehyde with oxocyclopentathiophenes or oxatetrahydroquinolines were prepared I had min. inhibitory concns. of 0.02-12.5 μ g/ml in vitro against Trichomonas vaginalis.
CC 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 22, 1
IT 57311-39-4P 57311-40-7P 57311-41-8P 57311-42-9P 57311-43-0P
57311-44-1P 57311-45-2P 57311-46-3P 57311-47-4P 57311-48-5P
57311-49-6P 57311-50-9P 57311-51-0P 57311-52-1P
57311-53-2P 57311-54-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and trichomonacidal activity of)
IT 57311-50-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and trichomonacidal activity of)
RN 57311-50-9 HCAPLUS
CN 2,5(1H,6H)-Quinolinedione, 7,8-dihydro-6-[(1-methyl-5-nitro-1H-imidazol-2-yl)methylene]- (CA INDEX NAME)



L88 ANSWER 39 OF 42 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1954:35986 HCAPLUS Full-text
DOCUMENT NUMBER: 48:35986
ORIGINAL REFERENCE NO.: 48:6443h-i,6444a-b
TITLE: Quinoline derivatives
AUTHOR(S): Sastry, K. N. S.; Bagchi, P.
CORPORATE SOURCE: Indian Assoc. Cultivation Sci., Jadavpur, Calcutta
SOURCE: Science and Culture (1953), 18, 543-5
CODEN: SCINAL; ISSN: 0036-8156
DOCUMENT TYPE: Journal

LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB Several quinoline derivs. were prepared p-H2NC6H4CH2CN refluxed in equimolar proportions with AcCH2CO2Et 3 hrs. at 180° gave a white anilide (I), m. 222°; semicarbazone, m. 252°. Attempted cyclization of I in paraffin at 250° was unsuccessful. However cyclization occurred in concentrated H2SO4 in 15 min. at 95°, giving 2-hydroxy-4-methyl-6-(cyanomethyl)quinoline, m. 258° (from alc.). The 4-Me group reacted with aldehydes, giving styryl and p-methoxystyryl derivs., m. 126° and 142°, resp. p-Toluidine and AcCH2CO2Et heated 3 hrs. at 170° gave an anilide, m. 185° (from alc.); semicarbazone, m. 218°. The same cyclization technique gave 2-hydroxy-4,6-dimethylquinoline (II), m. 224° (from alc.). 4-Styryl derivative of II m. 262° (from alc.). With benzoin, II gave 2-(2-hydroxy-6-methyl-4-quinolylmethylene)-1,2-diphenylethyl alc. m. 142° (from alc.). 2-Hydroxy-3-dichloromethyl-4,6-dimethylquinoline, m. 258° (from alc.), is also obtained from II. 4,2-Me(O2N)C6H3NH2 condensed with AcCH2CO2Et gave an anilide (III), m. 139° (from alc.), cyclized in concentrated H2SO4 gave 2-hydroxy-4,6-dimethyl-8-nitroquinoline, m. 174°. p-O2NC6H4NH2, m-O2NC6H4NH2, and o-H2NC6H4OH anilides m. 184°, 158°, and 128°, resp., which could not be cyclized. p-H2NC6H4CH2CO2H and 3,5,4-Br2MeC6H2NH2 did not condense with AcCH2CO2Et.
CC 10 (Organic Chemistry)
IT 2415-85-2P, p-Acetoacetotoluidide 4835-39-6P, Acetoacetanilide, 4'-nitro- 22016-02-0P, Acetoacetanilide, 2'-hydroxy- 23947-37-7P, Carbostyril, 4,6-dimethyl- 25233-49-2P, Acetoacetanilide, 3'-nitro- 34797-70-1P, p-Acetoacetotoluidide, 2'-nitro- 630110-25-7P, p-Acetoacetotoluidide, semicarbazone 854826-91-8P, Carbostyril, 4-(3-hydroxy-2,3-diphenylpropenyl)-6-methyl- 854826-91-8P, 2-Propen-1-ol, 3-(2-hydroxy-6-methyl-4-quinolyl)-1,2-diphenyl- 854834-92-7P, Carbostyril, 4,6-dimethyl-8-nitro- 855733-85-6P, Carbostyril, 3-(dichloromethyl)-4,6-dimethyl- 855734-22-4P, Carbostyril, 6-methyl-4-styryl- 860204-35-9P, 6-Quinolineacetonitrile, 2-hydroxy-4-styryl- 860717-02-8P, 6-Quinolineacetonitrile, 2-hydroxy-4-methyl- 860717-71-1P, 6-Quinolineacetonitrile, 2-hydroxy-4-(p-methoxystyryl)- 861067-82-5P, p-Acetoacetotoluidide, α-cyano-, semicarbazone 861067-84-7P, p-Acetoacetotoluidide, α-cyano-
RL: PREP (Preparation)
(preparation of)
IT 860717-02-8P, 6-Quinolineacetonitrile, 2-hydroxy-4-methyl-
RL: PREP (Preparation)
(preparation of)
RN 860717-02-8 HCAPLUS
CN 6-Quinolineacetonitrile, 1,2-dihydro-4-methyl-2-oxo- (CA INDEX NAME)



=> d iall abeq tech abex hitstr 40-42
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX' - CONTINUE? (Y)/N:y

L88 ANSWER 40 OF 42 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2005-747026 [76] WPIX
DOC. NO. CPI: C2005-227572 [76]
TITLE: New 2,3,4,5-tetrahydro-1H-benzo(d)azepine compounds are muscarinic acetylcholine receptor antagonists useful to treat e.g. chronic obstructive lung disease, allergic rhinitis, gastrointestinal tract disorder and urinary-tract disorder
DERWENT CLASS: B02
INVENTOR: BUSCH-PETERSEN J; LAINE D I; PALOVICH M R; LAINE D; PALOVICH M
PATENT ASSIGNEE: (GLAX-C) GLAXO GROUP LTD; (BUSC-I) BUSCH-PETERSEN J; (LAIN-I) LAINE D I; (PALO-I) PALOVICH M R
COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005094835	A1	20051013	(200576)*	EN	104[0]	
EP 1725241	A1	20061129	(200680)	EN		
US 20070185088	A1	20070809	(200754)	EN		
JP 2007529514	W	20071025	(200780)	JA	94	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005094835	A1	WO 2004-US8032	20040317
EP 1725241	A1	EP 2004-821848	20040317
EP 1725241	A1	WO 2004-US8032	20040317
US 20070185088	A1	WO 2004-US8032	20040317
US 20070185088	A1	US 2006-598888	20060914
JP 2007529514	W	WO 2004-US8032	20040317
JP 2007529514	W	JP 2007-503878	20040317

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1725241	A1	Based on	WO 2005094835 A
JP 2007529514	W	Based on	WO 2005094835 A

PRIORITY APPLN. INFO: WO 2004-US8032 20040317
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-55 [I,A]; A61K0031-55 [I,A]; A61K0031-55 [I,C]; A61K0031-55 [I,C]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0001-06 [I,A]; A61P0001-08 [I,A]; A61P0001-14 [I,A]; A61P0011-00 [I,A]; A61P0011-00 [I,C]; A61P0011-02 [I,A]; A61P0011-06 [I,A]; A61P0013-00 [I,C]; A61P0013-02 [I,A]; A61P0013-10 [I,A]; A61P0025-00 [I,C]; A61P0025-04 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; C07D0223-00 [I,C]; C07D0223-00 [I,C]; C07D0223-16 [I,A]; C07D0223-16 [I,A]; C07D0401-00 [I,C]; C07D0401-04 [I,A]; C07D0401-12 [I,A]; C07D0403-00 [I,C]; C07D0403-02 [I,A]; C07D0403-04 [I,A]; C07D0403-12 [I,A]; C07D0405-00 [I,C]; C07D0405-12 [I,A]; C07D0409-00 [I,C]; C07D0409-12 [I,A]; C07D0413-00 [I,C];

C07D0413-04 [I,A]; C07D0413-12 [I,A]; C07D0413-14 [I,A]; C07D0417-00 [I,C]; C07D0417-02 [I,A]; C07D0417-12 [I,A]; C07D0471-00 [I,C]; C07D0471-04 [I,A]

IPC RECLASSIF.: A61K0031-55 [I,A]; A61K0031-55 [I,C]; A61P0011-00 [I,A]; A61P0011-00 [I,C]; C07D0223-00 [I,C]; C07D0223-16 [I,A]

USCLASS NCLM: 514/217.010

NCLS: 540/594.000

JAP. PATENT CLASSIF.:

MAIN/SEC.: A61K0031-55; A61P0001-04; A61P0001-06; A61P0001-08; A61P0001-14; A61P0011-00; A61P0011-02; A61P0011-06; A61P0013-02; A61P0013-10; A61P0025-04; A61P0043-00 111; C07D0401-04; C07D0401-12; C07D0403-04; C07D0403-12; C07D0405-12; C07D0409-12; C07D0413-04; C07D0413-12; C07D0413-14; C07D0417-12; C07D0471-04 104 Z; C07D0223-16 Z (CSP)

FTERM CLASSIF.: 4C034; 4C063; 4C065; 4C086; 4C201; 4C063/AA01; 4C086/AA01; 4C086/AA02; 4C063/AA03; 4C086/AA03; 4C065/AA04; 4C063/BB01; 4C065/BB04; 4C063/BB09; 4C086/BC32; 4C086/BC39; 4C086/BC52; 4C086/BC67; 4C086/BC69; 4C086/BC70; 4C086/BC71; 4C086/BC84; 4C086/CB05; 4C065/CC01; 4C063/CC19; 4C063/CC22; 4C063/CC26; 4C063/CC29; 4C063/CC34; 4C063/CC51; 4C063/CC52; 4C063/CC58; 4C063/CC75; 4C063/CC76; 4C063/CC81; 4C063/CC82; 4C063/CC92; 4C063/CC94; 4C065/DD02; 4C063/DD04; 4C063/DD06; 4C063/DD12; 4C063/DD19; 4C034/DQ03; 4C063/EE01; 4C065/EE02; 4C086/GA02; 4C086/GA04; 4C086/GA07; 4C086/GA08; 4C086/GA09; 4C086/GA10; 4C086/GA12; 4C086/GA16; 4C065/HH01; 4C065/JJ01; 4C065/KK08; 4C065/LL01; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C065/PP04; 4C065/PP08; 4C065/PP16; 4C086/ZA29; 4C086/ZA34; 4C086/ZA59; 4C086/ZA66; 4C086/ZA68; 4C086/ZA71; 4C086/ZA73; 4C086/ZA81; 4C086/ZB13; 4C086/ZC41; 4C086/ZC42

BASIC ABSTRACT:

WO 2005094835 A1 UPAB: 20060125

NOVELTY - 2,3,4,5-Tetrahydro-1H-benzo(d)azepine compounds (I) and their salts are new.

DETAILED DESCRIPTION - 2,3,4,5-Tetrahydro-1H-benzo(d)azepine compounds of formula (I) and their salts are new.

R1 = H, halo, OH, CN, NO2, CF3, OCF3, trifluoromethanesulfonyloxy, pentafluoroethyl, 1-4C alkyl, 1-4C alkoxy, aryl1-4C alkoxy, 1-4C alkylthio, 1-4C alkoxyl-4C alkyl, 3-6C cycloalkyl1-4C alkoxy, 1-4C alkoxycarbonyl, 1-4C alkylsulfonyl, 1-4C alkylsulfonyloxy, 1-4C alkylsulfonyl1-4C alkyl, arylsulfonyl, arylsulfonyloxy, arylsulfonyl1-4C alkyl, 1-4C alkylsulfonamido, 1-4C alkylamido, 1-4C alkylsulfonamido1-4C alkyl, 1-4C alkylamido1-4C alkyl, arylsulfonamido, arylcarboxamido, arylsulfonamido1-4C alkyl, arylcarboxamido1-4C alkyl group, R3OCO(CH2)p, R3CON(R4)(CH2)p, R3R4NCO(CH2)p, R3R4NSO2(CH2)p or Ar3-Z; either

R3, R4 = H or 1-4C alkyl; or

R3R4 = 3-6C azacycloalkane or 3-6C (2-oxo)azacycloalkane ring;

p = 0-4;

Ar1-Ar3 = phenyl ring or 5-6 membered aromatic heterocyclic ring (both optionally substituted);

Z = bond, O, S or CH2;

R2 = H or 1-4C alkyl;

q = 1-2;

A = -Ar, -Ar1-Y-Ar2, -CH=CH-Ar or (CH2)r-V1-(CH2)sAr;

Ar = phenyl ring, 5-6 membered aromatic heterocyclic ring or bicyclic ring system (all optionally substituted);

Y = bond, -NHCO-, -CONH-, -CH2- or -(CH2)mY1(CH2)n;
Y1 = O, S, SO2 or CO; either
m, n = 0-1; or
m+n = 0-1; either
r, s = 0-3; or
r+s = 1-4; and
V1 = bond, O or S.
Provided that when A = -Ar, then any substituent present in Ar ortho to the carboxamide moiety is H or OCH3.

ACTIVITY - Respiratory-Gen.; Antiinflammatory; Antiasthmatic; Thrombolytic; Antiallergic; Gastrointestinal-Gen.; Antiulcer; Anticonvulsant; Analgesic; Uropathic; Antiemetic.

MECHANISM OF ACTION - M3 Muscarinic acetylcholine receptor antagonist.

Test details are described but no results given.

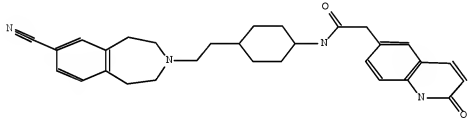
USE - (I) are useful for the treatment of muscarinic acetylcholine receptor mediated diseases such as chronic obstructive lung disease, chronic bronchitis, asthma, chronic respiratory obstruction, pulmonary fibrosis, pulmonary emphysema and allergic rhinitis (claimed). (I) are also useful to treat e.g. gastrointestinal tract disorders e.g irritable bowel syndrome, spasmodic colitis, gastroduodenal ulcers, gastrointestinal convulsions or hyperanakinesia, diverticulitis, pain accompanying spasms of gastrointestinal smooth musculature; urinary-tract disorders accompanying micturition disorders including neurogenic pollakisuria, neurogenic bladder, nocturnal enuresis, psychosomatic bladder, incontinence associated with bladder spasms or chronic cystitis, urinary urgency or pollakiuria, and motion sickness. MANUAL CODE: CPI: B06-D04; B14-E05; B14-E08; B14-E10; B14-G02A; B14-J02B1; B14-J02B2; B14-K01; B14-N04; B14-N07D; B14-N09; N05-C

TECH

ORGANIC CHEMISTRY - Preparation: Preparation of (I) comprises:
(A) reacting an azepine derivative of formula (II) with an acid halide (III) of formula A-COX (where X = halo or the residue of an activated ester); or
(B) reacting (II) with a halo derivative of formula A-Br or A-I, or a sulfonyloxy halide of formula A-OSO2CF3 in the presence of carbon monoxide and a catalyst such as trans-bis-triphenylphosphinepalladium (II) bromide; or
(C) (where R1 is Ar3-Z and Z is bond) reacting an azepine derivative of formula (IV) (where one R1a is a group W, where W = a halo or a trifluoromethylsulfonyl group, or W = a group M, where M is a boron derivative e.g. a boronic acid function B(OH)2 or a metal function such as trialkylstannyl e.g. SnBu3, zinc halide or magnesium halide, and when q is 2 the other R1a is R1), with a halo or sulfonyloxy compound of formula Ar3-W1 (where W1 is halo or trifluoromethylsulfonyloxy group when W is a group M or W1 is group M when W is a halo or trifluoromethylsulfonyloxy group); or
(D) (where R1 is Ar3-Z and Z is O or S) reacting an azepine derivative of formula (V) (where R1b is ZH and when q is 2 the other R1b is R1) with a reagent serving to introduce the group Ar3; or
(E) (where Y is a bond) reacting an azepine derivative of formula (VI) with halo or sulfonyloxy compound Ar2-W1 (where W1 is halo or trifluoromethylsulfonyloxy group when W is a group M, or W1 is a group M when W is a halo or a trifluoromethylsulfonyloxy group); and
(F) interconverting one compound of formula (I) to a different compound of formula (I).

ABEX ADMINISTRATION - Administration of (I) is via inhalation via the mouth or nose; or via a medicament dispenser such as a reservoir dry powder inhaler, a multi-dose dry powder inhaler or a metered dose inhaler. The duration of action of (I) when administered to a human is 12 hours or more for a 1mg dose or 36 hours or more (claimed). Dosage is 20 micrograms to

10 mg.
SPECIFIC COMPOUNDS - 145 Compounds (I) are specifically claimed e.g. trans-(E)-7-cyano-3-(2-(1-(4-(5-quinolinyl)carboxamido)cyclohexyl)ethyl)-2,3,4,5-tetrahydro-1H-benzazepine (Ia).
EXAMPLE - A mixture of trans-3-(2-(1-(4-amino)cyclohexyl)ethyl)-7-cyano-2,3,4,5-tetrahydro-1H-benzazepine (0.10 g), quinoline-5-carboxylic acid (0.057 g), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (0.065 g), 1-hydroxybenzotriazole (catalytic amount) and dichloromethane (8 ml) was shaken for 16 hours. Saturated sodium bicarbonate (4 ml) was then added and the mixture shaken for 0.25 hour. Chromatography on the organic layer on silica eluting with a gradient of 30-100% ethyl acetate in hexane and then 0-10% methanol in ethyl acetate gave trans-(E)-7-cyano-3-(2-(1-(4-(5-quinolinyl)carboxamido)cyclohexyl)ethyl)-2,3,4,5-tetrahydro-1H-benzazepine (Ia) (0.130 g, 86%).
AN.S DCR-1173743
CN.S N-{4-[2-(7-Cyano-1,2,4,5-tetrahydro-3-benzazepin-3-yl)-ethyl]-cyclohexyl}-2-(2-oxo-1,2-dihydro-quinolin-6-yl)-acetamideN-{4-[2-(7-Cyano-1,2,4,5-tetrahydro-benzo[d]azepin-3-yl)-ethyl]-cyclohexyl}-2-(2-oxo-1,2-dihydro-quinolin-6-yl)-acetamide
SDCN RAJWHA



L88 ANSWER 41 OF 42 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2004-097377 [10] WPIX
CROSS REFERENCE: 1991-073303; 1992-064851; 2004-439861
DOC. NO. CPI: C2004-040443 [10]
TITLE: Conjugate useful for the treatment of hypertensive related disorder and sodium-retaining disorder comprises two residues, which are connected together by a cleavable bond
DERWENT CLASS: B05
INVENTOR: BLAINE E H; KOEPKE J P; MANNING R E; REITZ D B; SCHUH J R; SMITS G J
PATENT ASSIGNEE: (SEAR-C) SEARLE & CO G D
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20030220521	A1	20031127	(200410)*	EN	151	[16]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030220521	A1 CIP of	US 1989-386527	19890727
US 20030220521	A1 CIP of	WO 1990-US4168	19900725
US 20030220521	A1 Cont of	US 1994-280170	19940725
US 20030220521	A1 Cont of	US 1996-639493	19960429
US 20030220521	A1 Cont of	US 1999-444888	19991122
US 20030220521	A1 Cont of	US 2000-678015	20001002
US 20030220521	A1	US 2002-151211	20020520

PRIORITY APPLN. INFO: US 2002-151211 20020520
US 1989-386527 19890727
WO 1990-US4168 19900725
US 1994-280170 19940725
US 1996-639493 19960429
US 1999-444888 19991122
US 2000-678015 20001002

INT. PATENT CLASSIF.:
IPC RECLASSIF.: C07C0237-00 [I,C]; C07C0237-12 [I,A]; C07C0237-22 [I,A];
C07C0059-00 [I,C]; C07C0059-64 [I,A]; C07C0059-90 [I,A];
C07D0209-00 [I,C]; C07D0209-08 [I,A]; C07D0209-20 [I,A];
C07D0209-34 [I,A]; C07D0213-00 [I,C]; C07D0213-50 [I,A];
C07D0213-65 [I,A]; C07D0213-73 [I,A]; C07D0213-80 [I,A];
C07D0213-81 [I,A]; C07D0213-86 [I,A]; C07D0215-00 [I,C];
C07D0215-22 [N,A]; C07D0215-227 [I,A]; C07D0233-00 [I,C];
C07D0233-54 [I,A]; C07D0233-88 [I,A]; C07D0233-90 [I,A];
C07D0235-00 [I,C]; C07D0235-30 [I,A]; C07D0241-00 [I,C];
C07D0241-42 [I,A]; C07D0241-44 [I,A]; C07D0263-00 [I,C];
C07D0263-58 [I,A]; C07D0265-00 [I,C]; C07D0265-36 [I,A];
C07D0285-00 [I,C]; C07D0285-14 [I,A]; C07D0307-00 [I,C];
C07D0307-46 [I,A]; C07D0307-52 [I,A]; C07D0333-00 [I,C];
C07D0333-20 [I,A]; C07D0333-22 [I,A]; C07D0333-66 [I,A]
ECLA: C07C0059-64; C07C0059-90; C07C0237-12; C07C0237-22;
C07D0209-08; C07D0209-20; C07D0209-34; C07D0213-50;
C07D0213-65; C07D0213-73D; C07D0213-80B3; C07D0213-81E;
C07D0213-86F; C07D0215-22B; C07D0233-54C2D4;
C07D0233-54C2D5; C07D0233-88; C07D0233-90; C07D0235-30;
C07D0241-42; C07D0241-44; C07D0263-58D; C07D0265-36;
C07D0285-14D; C07D0307-46; C07D0307-52; C07D0333-20;
C07D0333-22; C07D0333-66
ICO: M07D0209:08; M07D0209:20; M07D0209:34; M07D0213:50;
M07D0213:65; M07D0213:73D; M07D0213:80B3; M07D0213:81E;
M07D0213:86F; M07D0215:22B; M07D0233:54C2D4;
M07D0233:54C2D5; M07D0233:88; M07D0233:90; M07D0235:30;
M07D0263:58D
USCLASS NCLM: 562/450.000
BASIC ABSTRACT:

US 20030220521 A1 UPAB: 20050528

NOVELTY - A conjugate comprises two residues, which are connected together by a cleavable bond. The first residue is provided by an inhibitor compound capable of inhibiting biosynthesis of an adrenergic neurotransmitter. The second residue is cleaved from the first residue by an enzyme located predominantly in the kidney.

ACTIVITY - Hypotensive; Cardiant; Hepatotropic; Nephrotropic.

An experimental assay was carried out to determine the effect of N-(4-(acetylamino)-4-carboxy-1-oxobutyl)-3-hydroxy-alpha-methyl-L- tyrosine (test compound)/saline vehicle on the hypertensive rats as follows: The test compound (10 mg/hour)/vehicle (300 microl/hour) was infused continuously for four days in spontaneously hypertensive rats. The mean arterial pressure was

measured via an indwelling femoral artery catheter between 10 a.m. - 2 p.m. each day. The mean arterial pressure (mm Hg) of the test/control rats was 179+/-6/181+/-8 (in the beginning); 169+/-5/172+/-6 (after one day); 161+/-4/170+/-7 (after 2 days); 163+/-5/174+/-6 (after 3 days); and 159+/-8/182+/-3 (after 4 days).

MECHANISM OF ACTION - Tyrosine hydroxylase inhibitor; Dopa-decarboxylase inhibitor; Dopamine-beta-hydroxylase inhibitor.

USE - For the treatment of hypertensive related disorder (e.g. chronic hypertension) and sodium retaining disorder (e.g. congestive heart failure, cirrhosis and nephrosis) (all claimed).

ADVANTAGE - The conjugates prevent adverse side effects. The conjugates selectively inhibit renal sympathetic nerve activity and lower blood pressure.

MANUAL CODE: CPI: B06-H; B07-H; B14-F01E; B14-F02B; B14-N10; B14-N12

TECH

ORGANIC CHEMISTRY - Preferred Components: The first and the second residue are provided by the precursor compounds. The precursor compound of one of the first and the second residues has a reactable carboxylic acid moiety and the precursor of the other of the first and the second residues has a reactable amino moiety or a moiety convertible to a reactable amino moiety. A cleavable bond is formed between the carboxylic acid moiety and the amino moiety. The precursor compound providing the second residue has a reactable acid moiety. The second residue precursor compound of the conjugate is selected from a class of glutamic acid derivative of formula GCCH2CH2CH-(C(O)G)(NR150R151). The first and the second residues are connected through a cleavable bond provided by a linker group between the first and the second residues. 4 Linker groups, L1-L4 are given.

R150 = q1 (preferably hydrido);

q1 = hydrido, alkylcarbonyl, alkoxycarbonyl, alkoxyalkyl, hydroxyalkyl or haloalkyl;

R151 = q1 (preferably C(O)R155);

R155 = methyl, ethyl, n-propyl, isopropyl, n-butyl, sec butyl, isobutyl, tert butyl, n-pentyl, neopentyl, n-hexyl or chloromethyl;

G = OH, halo, mercapto, OR152, SR153 or NR154 (preferably OH);

R152 - R154 = hydrido or alkyl;

n1 = 0 - 7 (preferably 0);

R200 and R201 = hydrido, alkyl, cycloalkyl, cycloalkylalkyl, alkoxyalkyl, hydroxyalkyl, aralkyl, aryl, haloalkyl, amino, monoalkylamino, dialkylamino, cyanoamino, carboxyalkyl, alkylsulfino, alkylsulfonyl, arylsulfinyl or arylsulofnyl (preferably hydrido).

Provided that the glutamic acid derivative is selected such that the formation of the cleavable bond occurs at the carbonyl moiety attached at the gamma-position carbon of the gamma glutamic acid derivative.

PHARMACEUTICALS - Preferred Components: The inhibitor compound providing the first residue is selected from tyrosine hydroxylase inhibitor, dopa-decarboxylase inhibitor or dopamine-beta-hydroxylase inhibitor or mimics of the inhibitor. The tyrosine hydroxylase inhibitor is a compound of formula (T1) or its salt. 5 dopamine-beta-hydroxylase inhibitors are given e.g. a compound of formula (B1) or its salt. The dopa-decarboxylase inhibitor is a compound selected from amino-haloalkyl-hydroxyphenyl propionic acid, alpha-halomethyl-phenylalanine derivative, indole-substituted halomethylamino acid, isoflavone extract from fungi and streptomyces, sulfinyl substituted dopa and tyrosine derivative, hydroxycoumarin derivative, 1-benzylcyclobutenyl alkyl carbamate derivative, aryl/thienyl-hydroxylamine derivative, or b-2-substituted-cyclohepta-pyrrol-8-1H-on-7-yl alanine derivative, e.g. (D1) or their salt. The first residue is provided by a dopa-decarboxylase inhibitor compound, dopamine-beta-hydroxylase inhibitor compound or tyrosine hydroxylase inhibitor compound and the second residue is provided by a gamma glutamic acid derivative.

R4, R21,R22 = T3;
R36 - R47 = hydrido, hydroxy, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl, aryl, alkoxy, aralkoxy, alkoxyalkyl, haloalkyl, hydroxalkyl, halo, cyano, amino, monoalkylamino, dialkylamino, carboxyl, carboxyalkyl, alkanoyl, alkenyl, cycloalkenyl, alkynyl, cyanoamino, cyano, thiocarbamoyl, aminomethyl, alkylsulfanamido, nitro, alkylsulfonyloxy, carboxyalkoxy or formyl;
R14 - R20 = Q1, cyanoamino, carboxyl, cyano, thiocarbamoyl, aminomethyl, alkylsulfanamido, nitro, alkylsulfonyloxy, carboxyalkoxy or formyl;
R1 - R2 = T1;
T1 = Q1 or aryloxy;
Q1 = hydrido, hydroxy, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl, aryl, alkoxy, aralkoxy, alkoxyalkyl, haloalkyl, hydroxyalkyl, halo, cyano, amino, monoalkylamino, dialkylamino, carboxyl, carboxyalkyl, alkanoyl, alkenyl, cycloalkenyl or alkynyl;
R3 = T1 or T2;
T3 = hydrido, alkyl, cycloalkyl, hydroxyalkyl, haloalkyl, cycloalkylalkyl, alkoxyalkyl, aralkyl, aryl, alkanoyl, alkoxycarbonyl, carboxyl, amino, cyanoamino, monoalkylamino, dialkylamino, alkylsulfinyl, alkylsulfonyl, arylsulfinyl or arylsulfonyl;
R5 = OR6 or NR7R8;
R6 = hydrido, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl or aryl;
R7, R8 = T2;
T2 = T3 or aralkyl;
A = phenyl (substituted by R9 - R13 at positions 1 - 5), a group of formula (ia) or 1H-imidazole (substituted by at positions 2 and 5 by R19 and R20 respectively)(ib) or -NR21R22;
R9 - R13 = Q1, cyanoamino, carboxyl, cyano, thiocarbamoyl, aminomethyl, alkylsulfanamido, nitro, alkylsulfonyloxy, catboxyalkoxy, formyl or optionally substituted 5- or 6-membered heterocyclic ring selected from T4;
T4 = pyrrol-1-yl, 2-carboxypyrrol-1-yl, imidazol-2-ylamino, indol-1-yl, carbozol-9-yl, 4,5-dihydro-4-hydroxy-4-trifluoro-methylthiazol-3-yl, 4-trifluoromethylthiazol-2-yl, imidazol-2-yl or 4,5-dihydroimidazol-2-yl;
2(R9+R13) = benzoheterocyclic ring selected form indoin-5-yl, 1-(N-benzoylcarbamimidoyl)indolin-5-yl, 1-carbamimidoylindolin-5-yl, 1H-2-oxindol-5-yl, insol-5-yl, 2-mercaptobenimidazol-5(6)-yl, 2-aminobenzimidazol-5-(6)-yl, 2-methanesulfonamidobenzimidazol-5(6)-yl, 1H-benzoxanol-2-on-6-yl, 2-aminobenzothiazol-6-yl, 2-amino-4-mercaptobenzothiazol-6-yl, 2,1,3-benzothiadiazol-5-yl, 1,3-dihydro-2,2-dioxo-2,1,3-benzothiadiazol-5-yl, 1,3-dihydro-1,3-dimethyl-2,2-dioxo-2,1,3-benzothiadiazol-5-yl, 4-methyl-2(H)oxoquinolin-6-yl, quinoxalin-6-yl, 2-hydroxyquinoxalin-6-yl, 2-hydroxyquinoxalin-7-yl, 2,3-dihydroxyquinoxalin-6-yl or 2,3-dihydro-3(4H)-oxo-1,4-benzoxazin-7-yl, 5-hydroxy-4H-pyran-4-on-2-yl, 2-hydroxypyrid-4-yl, 2-aminopyrid-4-yl, 2-carboxyprid-4-yl or tetrazolo(1,5-a)pyrid-7-yl;
R112 = T5 (preferably mercapto, alkylthio, amino, aminoalkyl, monoalkylamino, monoalkylaminoalkyl, carboxy or carboxyalkyl);
T5 = hydrido, hydroxy, alkyl, cycloalkyl, cycloalkylalkyl, alkoxy, alkoxyalkyl, aralkyl, aryl, alkoxycarbonyl, hydroxyalkyl, halo, haloalkyl, cyano, amino, aminoalkyl, monoalkylamino, dialkylamino, carboxyl, carboxyalkyl, alkanoyl, alkenyl, cycloalkenyl, alkynyl, mercapto or alkylthio;
R113 - R115 and R119 = T5 (preferably hydrido);
R116 - R118 = T5 (preferably hydrido, hydroxy, alkyl or (halo)alkyl);
R52 = hydrido, OR64 or -NR65R66 (preferably OR64);
R64 = hydrido, alkyl, cycloalkyl, cycloalkylalkyl, phenalkyl or phenyl (preferably hydrido or lower alkyl);
R65 and R66 = hydrido, alkyl, alkanoyl, amino, monoalkylamino,

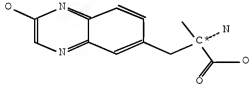
dialkylamino, phenyl or phenylalkyl;
R53 and R54, R57 and R58 = T6 (preferably hydrido);
T6 = hydrido, hydroxy, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl, aryl, alkoxycarbonyl, hydroxyalkyl, halo, cyano, amino, monoalkylamino, dialkylamino, carboxyl, carboxyalkyl, alkanoyl, alkenyl, cycloalkenyl or alkynyl;
R55 and R56 = T6, hydrido, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl, aryl, alkoxyalkyl, haloalkyl, hydroxyalkyl or carboxyalkyl (preferably hydrido);
R59 - R63 = T6 (preferably hydrido, alkyl, hydroxy or alkoxy);
co = 0 - 6 (preferably 0 - 2).
Provided that two of the R59 - R63 substituents are OH.

ABEX ADMINISTRATION - The conjugates are administered intravascularly, intraperitoneally, subcutaneously, intramuscularly, topically or orally. Tablets or capsules comprise 1 - 250 (preferably 25 - 150) mg of the conjugates. A daily dosage of the conjugates is 0.1 - 3000 (preferably 1 - 100) mg/kg. For injection, the daily dosage of the conjugate is 0.1 - 100 (preferably 1 - 30) mg/kg. For treatment purposes, the daily dosage of the conjugates is 0.1 - 100 (preferably 1 - 100, especially 1 - 50) mg/kg. A per unit dosage of the conjugate is 1 - 100 (preferably 2 - 50, especially 3 - 25) mg.

SPECIFIC COMPOUNDS - 298 Compounds are specifically claimed as the inhibitor compounds e.g. 4-cyanoamino-a-methylphenylalanine (Ia). 21 Compounds are specifically claimed as the conjugate e.g. N-(4-(acetylamino)-4-carboxy-1-oxobutyl)-3-hydroxy-alpha-methyl-L-tyrosine.

EXAMPLE - A solution of N-(4-(acetylamino)-4-carboxy-1-oxobutyl)-3-hyroxy-alpha-methyl-L-tyrosine, methyl ester (13.5 g) in water (34 ml) was cooled to 0degreesC and treated with 1N NaOH (102 ml). The resulting reaction mixture was stirred at ambient temperature for 5 hours and then worked up to form N-(4-(acetylamino)-4-carboxy-1-oxobutyl)-3-hydroxy-alpha-methyl-L-tyrosine (68%) as a colorless product.

AN.S DCR-828546
CN.S 2-Amino-3-(2-hydroxy-quinoxalin-6-yl)-2-methyl-propionic acid
SDCN RACQIH



AN.S DCR-828542
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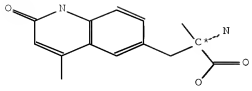

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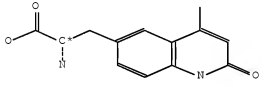

L88 ANSWER 42 OF 42 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2000-237838 [20] WPIX
DOC. NO. CPI: C2000-072495 [20]
TITLE: Alkynyl-substituted quinolin-2-one derivatives are farnesyl protein transferase inhibitors, useful as anticancer agents and in the treatment of psoriasis, malaria and hepatitis delta viral infection
DERWENT CLASS: B02
INVENTOR: LA GRECA D; LA GRECA S; LA GRECA S D; LYSSIKATOS J; LYSSIKATOS J P; LYSSIKATOS P; LA G S D
PATENT ASSIGNEE: (LGRE-I) LA GRECA S D; (LYSS-I) LYSSIKATOS J P; (PFIZ-C) PFIZER INC; (PFIZ-C) PFIZER PROD INC
COUNTRY COUNT: 86

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000012499	A1	20000309	(200020)*	EN	43[0]	
AU 9949254	A	20000321	(200031)	EN		
US 6150377	A	20001121	(200101)	EN		
BR 9913138	A	20010508	(200129)	PT		
NO 2001000964	A	20010426	(200131)	NO		
EP 1107963	A1	20010620	(200135)	EN		
US 6294552	B1	20010925	(200158)	EN		
CN 1314904	A	20010926	(200206)	ZH		
KR 2001072991	A	20010731	(200209)	KO		
HU 2001003228	A2	20020228	(200223)	HU		
MX 2001001992	A1	20010801	(200238)	ES		
ZA 2001001173	A	20020529	(200240)	EN	56	
CZ 2001000660	A3	20020515	(200241)	CS		
US 20020128287	A1	20020912	(200262)	EN		
JP 2002523504	W	20020730	(200264)	JA	73	
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DE 69930518	E	20060511 (200634)	DE	
DE 69930518	T2	20060921 (200662)	DE	
ES 2259237	T3	20060916 (200663)	ES	
CA 2341690	C	20070417 (200729)	EN	
CA 2578326	A1	20000309 (200734)	EN	

APPLICATION DETAILS:

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US 20020128287 A1	US 2001-900401 20010706
US 6579887 B2	US 2001-900401 20010706
CA 2578326 A1 Div Ex	CA 1999-2341690 19990806
CA 2578326 A1	CA 1999-2578326 19990806

FILING DETAILS:

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ES 2259237	T3	Based on	EP 1107963	A
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US 6579887	B2	Div ex	US 6150377	A
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PRIORITY APPLN. INFO:	US 1998-98145P 19980827
	US 1999-383755 19990826
	US 2000-628039 20000727
	US 2001-900401 20010706
INT. PATENT CLASSIF.:	
MAIN:	A61K031-47; C07D401-06; C07D401-10
SECONDARY:	C07D215-16
IPC ORIGINAL:	A61K0031-47 [I,A]; A61K0031-47 [I,A]; A61K0031-47 [I,C]; A61K0031-47 [I,C]; C07D0215-00 [I,C]; C07D0215-00 [I,C]; C07D0215-00 [I,C]; C07D0215-22 [I,A]; C07D0215-22 [I,A]; C07D0215-22 [I,A]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-06 [I,A]; C07D0401-06 [I,A]; C07D0401-06 [I,A]; C07D0401-10 [I,A]; C07D0401-14 [I,A]; C07D0401-14 [I,A]; C07F0007-00 [I,C]; C07F0007-00 [I,C]; C07F0007-00 [I,C]; C07F0007-08 [I,A]; C07F0007-08 [I,A]; C07F0007-18 [I,A]
IPC RECLASSIF.:	A61K0031-47 [I,A]; A61K0031-47 [I,C]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61P0013-00 [I,A]; A61P0013-00 [I,C]; A61P0017-00 [I,C]; A61P0017-06 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0009-00 [I,A]; A61P0009-00 [I,C]; C07D0215-00 [I,C]; C07D0215-22 [I,A]; C07D0401-00 [I,C]; C07D0401-06 [I,A]; C07D0401-10 [I,A]; C07D0401-14 [I,A]; C07F0007-00 [I,C]; C07F0007-08 [I,A]; C07F0007-18 [I,A]
ECLA:	C07D0401-10+233+215; C07D0401-14+249B+233+215; C07F0007-18C4B

USCLASS NCLM: 514/312.000
NCLS: 514/151.000; 546/157.000; 546/158.000
JAP. PATENT CLASSIF.:
MAIN/SEC.: A61K0031-4709; A61P0013-00; A61P0017-06; A61P0035-00; A61P0043-00 111; A61P0009-00; C07D0401-06; C07D0401-14
FTERM CLASSIF.: 4C063; 4C086; 4C201; 4C206; 4C063/AA01; 4C086/AA02; 4C063/AA03; 4C086/AA03; 4C063/BB04; 4C086/BC38; 4C086/BC60; 4C063/CC25; 4C063/CC41; 4C063/DD14; 4C063/EE01; 4C086/GA07; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA36; 4C086/ZA81; 4C086/ZA89; 4C086/ZB26; 4C086/ZC20

BASIC ABSTRACT:

WO 2000012499 A1 UPAB: 20060116

NOVELTY - Alkynyl-substituted quinolin-2-one derivatives (I), their salts, prodrugs or solvates, are new.

DETAILED DESCRIPTION - Alkynyl-substituted quinolin-2-one derivatives of formula (I), their salts, prodrugs or solvates, are new.

dotted line = optional bond

R1 = H, 1-10C alkyl, (CR13R14)qC(O)R12, (CR13R14)qC(O)OR15, (CR13R14)qOR12, (CR13R14)qSO2R15, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl ,optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q), all optionally substituted by 1 - 4 R6;

Het = 4-10 membered heterocyclic ring;

t = 0 - 5;

q = 1 - 5

Q = 6-10C aryl, 5-8C saturated cyclic group or Het;

R2 = halo, CN, C(O)OR15, 1-10C alkyl, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl ,optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q);

R3 - R7 = H, 1-10C alkyl (optionally substituted with 1 -3 Q1), 2-10C alkenyl (optionally substituted with 1 -3 Q1), halo, CN, nitro, CF3, OCF3, N3, OR12, C(O)R12, C(O)OR12, NR13C(O)OR15, OC(O)R12, NR13SO2R15, SO2NR12R13, NR13C(O)R12, C(O)NR12R13, NR12R13, CH=NOR12, S(O)jR12, (CR13R14)t(6-10C aryl (optionally fused to Q and optionally substituted with 1 -3 Q1)), (CR13R14)t-Het (optionally fused to Q and optionally substituted with 1 -3 Q1), (CR13R14)t(3-10C cycloalkyl (optionally fused to Q and optionally substituted with 1 -3 Q1)), and (CR13R14)Ctriple bondCR16;

at least 1 of R3 - R5 = (CR13R14)tCtriple bondCR16;

j = 0 -2;

Q1 = halo, CN, nitro, CF3, OCF3, N3, SO2NR12R13, C(O)R12, C(O)OR12, OC(O)R12, NR13C(O)OR15, NR13C(O)R12, C(O)NR12R13, NR12R13, OR12, 1-10C alkyl, 2-10C alkenyl, 2-10C alkynyl, (CR13R14)t(6-10C aryl), and (CR13R14)t-Het;

R8 = H, OR12, NR12R13, NR12C(O)R13, CN, C(O)OR13, SR12, (CR13R14)t-Het (optionally substituted with 1 - 3 R6), or 1-6C alkyl (optionally substituted with 1 - 3 R6);

R9 = (CR13R14)t-imidazolyl (optionally substituted with 1 - 2 R6);

R10, R11 = H, 1-10C alkyl (optionally substituted with 1 -3 Q1), 2-10C alkenyl (optionally substituted with 1 -3 Q1), halo, CN, nitro, CF3, OCF3, N3, OR12, C(O)R12, C(O)OR12, NR13C(O)OR15, OC(O)R12, NR13SO2R15, SO2NR12R13, NR13C(O)R12, C(O)NR12R13, NR12R13, CH=NOR12, S(O)jR12, (CR13R14)t(6-10C aryl (optionally fused to Q and optionally substituted with 1 -3 Q1)), (CR13R14)t-Het (optionally fused to Q and optionally substituted with 1 -3 Q1), (CR13R14)t(3-10C cycloalkyl (optionally fused to Q and optionally substituted with 1 -3 Q1)), and (CR13R14)Ctriple bondCR16;

R12 = H, 1-10C alkyl, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q), all except H optionally substituted with 1 - 3 Q1;

R13, R14 = H, or 1-6C alkyl;

where R13, R14 = as (CR13R14)q or (CR13R14)t each R13, R14 is independently defined for each iteration of q or t over 1;

R15 = 1-10C alkyl, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q), all optionally substituted with 1 - 3 Q1;

R16 = H, 1-10C alkyl, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q), SiR17R18R19, all except H optionally substituted with 1 - 3 Q1; and

R17 - R19 = 1-10C alkyl, (CR13R14)t(3-10C cycloalkyl optionally fused to Q), (CR13R14)t(6-10C aryl optionally fused to Q), or (CR13R14)t-Het (optionally fused to Q), all except H optionally substituted with 1 - 3 Q1.

INDEPENDENT CLAIMS are also provided for:

(1) a pharmaceutical composition for the treatment of abnormal cell growth comprising (I) in combination with an anti-tumor agent selected from mitotic inhibitors, alkylating agents, antimetabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, anti-hormones and anti-androgens; and

(2) a compound of formula (II).

ACTIVITY - Cytostatic; antipsoriatic; vasotropic; virucide; hepatotropic; protozoacide.

MECHANISM OF ACTION - Farnesyl protein transferase inhibitor.

Assay procedure is given, but no biological data (IC50 values) is given.

USE - (I) are used to treat abnormal cell growth, particularly cancer, especially cancer of the lung, bone, pancreas, skin, head or neck, uterus, ovaries, rectum, anal region, stomach, colon, breast, esophagus, small intestine, endocrine system, thyroid gland, parathyroid gland, adrenal gland, urethra, penis, prostate, bladder, kidney or ureter (sic), carcinoma of the fallopian tubes, endometrium, cervix, vagina, vulva, soft tissue, renal pelvis, renal cell carcinoma, Hodgkin's Disease, chronic or acute leukemia, lymphocytic lymphomas, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, or pituitary adenoma (all claimed). (I) are also used to treat a benign proliferative disease, especially psoriasis, benign, prostatic hypertrophy or restinosis, hepatitis delta virus or malarial infections (all claimed). MANUAL CODE: CPI: B05-B01B; B06-D02; B14-A02; B14-A03; B14-D06; B14-F01; B14-H01B; B14-N12; B14-N17C

TECH ORGANIC CHEMISTRY - Preparation: Claimed preparation of (I: R3 = ethynyl) comprises treating a compound of formula (III) with tetrabutylammonium fluoride (TBAF).

ABEX DEFINITIONS - Preferred Definitions: - R1 = H, 1-6C alkyl or cyclopropylmethyl; or - R1 = (CR13R14)t(3-10C cycloalkyl), preferably cyclopropylmethyl; - t = 0 -3; - R2 = H; - R3 = Ctriple bondCR16, preferably ethynyl; - R8 = NR12R13, OR12 or a heterocyclic group selected from triazolyl, imidazolyl, pyrazolyl or piperidinyl, where each heterocyclic group is optionally substituted by R6; preferably OH, amino or triazolyl; - R9 = imidazolyl optionally substituted by 1-6C alkyl; and - R4, R5, R10, R11 = H or halo.

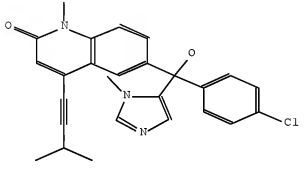
ADMINISTRATION - Administration is oral, transdermally, parenterally or topically, preferably oral. Dosage is 1 - 500 (preferably 1 - 100) mg/day, 0.01 - 10 mg/kg body weight/day in single or divided doses.

SPECIFIC COMPOUNDS - 5 Compounds (I) and 5 compounds (II) are specifically claimed, e.g. 6-((4-chlorophenyl)-hydroxy(3-methyl-3H-imidazol-4-yl)-methyl)-4-(3-ethynyl-4-fluorophenyl)-1-methyl-1H-quinolin-2-one of formula (Ia) and 6-(6-chlorobenzoyl)-1-cyclopropylmethyl-4-(3-trimethylsilanylethynylphenyl)-1H-quinolin-2-one (IIa).

EXAMPLE - 6-((4-Chlorophenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl)-1-methyl-4-(3-trimethylsilanylethynylphenyl)-1H-quinolin-2-one (3.88 g) was dissolved in tetrahydrofuran (THF; 10 ml) under an N2 atmosphere. To this was added a solution of 1.0 M tetrabutylammonium fluoride (TBAF) in

THF (20 ml). The reaction mixture was stirred at ambient temperature overnight and then concentrated under vacuum. The residue was partitioned between dichloromethane (DCM) and water. The DCM layer was washed 3 times with water and then with brine, dried over Na2SO4, filtered and concentrated under vacuum. The residue was chromatographed on flash silica gel eluting with a gradient from DCM to methanol/DCM (4:96) to give 6-((4-chlorophenyl)-hydroxy(3-methyl-3H-imidazol-4-yl)-methyl)-4-(3-ethynyl-4-fluorophenyl)-1-methyl-1H-quinolin-2-one (Ia) (3.01 g).

AN.S DCR-268933
CN.S 6-[(4-Chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-1-methyl-4-(3-methyl-but-1-ynyl)-1H-quinolin-2-one
SDCN RA1G3S



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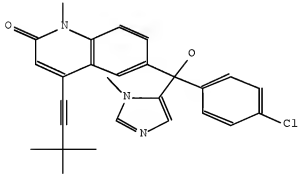

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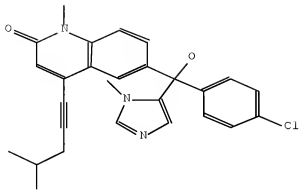

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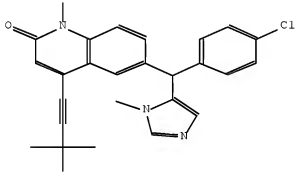
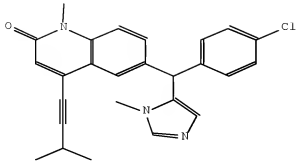
SDCN RA1G3V



AN.S DCR-268937
CN.S 6-[(4-Chloro-phenyl)-(3-methyl-3H-imidazol-4-yl)-methyl]-1-methyl-4-(3-methyl-but-1-ynyl)-1H-quinolin-2-one
SDCN RA1G3W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L35             QUE  SPE=ON  ABB=ON  PLU=ON  VANDUN, J?/AU
L36             QUE  SPE=ON  ABB=ON  PLU=ON  SOMERS, M?/AU
L37             QUE  SPE=ON  ABB=ON  PLU=ON  WOUTERS, W?/AU
L38             QUE  SPE=ON  ABB=ON  PLU=ON  JANSSEN/CS,SO,PA
L65             STR
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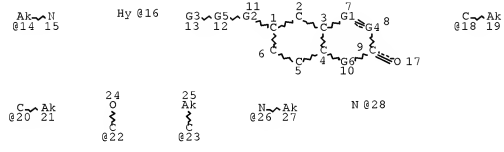


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REP G2=(0-3) C
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VAR G4=CH/18
VAR G5=CH/22/23
VAR G6=28/26
NODE ATTRIBUTES:
NSPEC   IS R      AT  28
CONNECT IS E2  RC AT  14
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  27
CONNECT IS E2  RC AT  28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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ECOUNT  IS X4 C  AT  14
ECOUNT  IS M2-X3 C  M2-X3 N  E0 O  E0 P  E0 S  E0 Si  AT  16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
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L79            7 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (RACQIC/DCN OR RACQID/DCN
                   OR RACQIH/DCN OR RAI9EX/DCN OR RAI9EZ/DCN OR RAI9F0/DCN OR
                  RAJWHA/DCN OR RAMT44/DCN OR RA1G3S/DCN OR RA1G3T/DCN OR
                  RA1G3U/DCN OR RA1G3V/DCN OR RA1G3W/DCN OR RA56SN/DCN OR
                  RA56SP/DCN OR RA56U2/DCN) OR L78/DCR
L80            3 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L79 AND (L32 OR L33 OR
                  L34 OR L35 OR L36 OR L37 OR L38)


=> d his l82

     (FILE 'MEDLINE, BIOSIS, EMBASE, CABA, BIOTECHNO, DRUGU, VETU, AGRICOLA'
     ENTERED AT 10:03:06 ON 08 JAN 2009)
L82            0 S L67

=> d que nos l82
L7               STR
L8  (    1332204)SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR
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L9         22147 SEA FILE=REGISTRY SUB=L8 SSS FUL L7
L65              STR
L67          429 SEA FILE=REGISTRY SUB=L9 SSS FUL L65
L82            0 SEA L67


=> d his l87

     (FILE 'MEDLINE, BIOSIS, EMBASE, PASCAL, CABA, CEABA-VTB, LIFESCI, BIOENG,
     BIOTECHNO, BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI,
     DISSABS, RDISCLOSURE' ENTERED AT 10:10:59 ON 08 JAN 2009)
L87            1 S L86 AND L32-L38

=> d que l87
L32              QUE  SPE=ON  ABB=ON  PLU=ON  MABIRE, D?/AU
L33              QUE  SPE=ON  ABB=ON  PLU=ON  GUILLEMONT, J?/AU
L34              QUE  SPE=ON  ABB=ON  PLU=ON  VAN DUN, J?/AU
L35              QUE  SPE=ON  ABB=ON  PLU=ON  VANDUN, J?/AU
L36              QUE  SPE=ON  ABB=ON  PLU=ON  SOMERS, M?/AU
L37              QUE  SPE=ON  ABB=ON  PLU=ON  WOUTERS, W?/AU
L38              QUE  SPE=ON  ABB=ON  PLU=ON  JANSSEN/CS,SO,PA
L83              QUE  SPE=ON  ABB=ON  PLU=ON  ?QUINOLINON? OR ?QUINOXALINO
                 N?
L84              QUE  SPE=ON  ABB=ON  PLU=ON  ADP
L85              QUE  SPE=ON  ABB=ON  PLU=ON  POLYMERAS?
L86          273 SEA L83 AND L84 AND L85
L87            1 SEA L86 AND (L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38)


=> dup rem l71 l80 l82 l87
L82 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'RDISCLOSURE'.
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ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'HCAPLUS' ENTERED AT 10:20:02 ON 08 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'WPIX' ENTERED AT 10:20:02 ON 08 JAN 2009
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FILE 'BIOTECHDS' ENTERED AT 10:20:02 ON 08 JAN 2009
COPYRIGHT (C) 2009 THOMSON REUTERS
PROCESSING COMPLETED FOR L71
PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L87
L89           9 DUP REM L71 L80 L82 L87 (1 DUPLICATE REMOVED)
                ANSWERS '1-6' FROM FILE HCAPLUS
                ANSWERS '7-8' FROM FILE WPIX
                ANSWER '9' FROM FILE BIOTECHDS

=> file stnguide
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USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan  6, 2009 (20090106/UP).
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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, BIOTECHDS' - CONTINUE? (Y)/N:y



L89  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:523430  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:60003
TITLE:                    Preparation of 6-substituted 2-quinolinones and
                          2-quinoxalinones as poly(ADP-ribose) polymerase
                          inhibitors
INVENTOR(S):              Mabire, Dominique Jean-Pierre;
                          Guillemont, Jerome Emile Georges; Van
                          Dun, Jacobus Alphonsus Josephus; Somers,
                          Maria Victorina Francisca; Wouters, Walter
                          Boudewijn Leopold
PATENT ASSIGNEE(S):       Janssen Pharmaceutica N. V., Belg.
SOURCE:                   PCT Int. Appl., 48 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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     WO 2005054210        A1    20050616    WO 2004-EP13164          20041118
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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             NE, SN, TD, TG
     AU 2004295059        A1    20050616    AU 2004-295059           20041118
     CA 2546657           A1    20050616    CA 2004-2546657          20041118
     EP 1709012           A1    20061011    EP 2004-819602           20041118
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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             HR, IS, YU
     CN 1890224           A     20070103    CN 2004-80035857         20041118
     BR 2004016532        A     20070109    BR 2004-16532            20041118
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     IN 2006DN03071       A     20070810    IN 2006-DN3071           20060529
     US 20070129375       A1    20070607    US 2006-596086           20060530
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     NO 2006003028        A     20060628    NO 2006-3028             20060628
PRIORITY APPLN. INFO.:                       EP 2003-78859        A  20031205
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OTHER SOURCE(S):          CASREACT 143:60003; MARPAT 143:60003
ED   Entered STN:  17 Jun 2005
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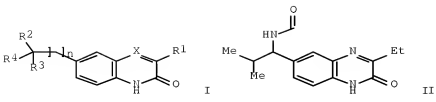

I II

AB The title compds. I [n = 0-2; X = N, CR5; R5 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thienyl; R2 = H, OH, or taken together with R3 or R4 may form O; R3 = OH, OR8, SR9, etc.; R8 = alkyl, alkylcarbonyl, dialkylaminoalkyl; R9 = dialkylaminoalkyl; R4 = H, alkyl, furanyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from 1-(4-amino-3-nitrophenyl)-2-methyl-1-propanone, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IC ICM C07D241-44
ICS C07D407-06; C07D401-12; C07D409-14; A61K031-498; A61P043-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 854523-79-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 854523-77-6P 854523-78-7P 854523-80-1P
854523-81-2P 854523-82-3P 854523-83-4P 854523-84-5P
854523-85-6P 854523-86-7P 854523-87-8P
854523-88-9P 854523-89-0P 854523-90-3P
854523-91-4P 854523-92-5P 854523-93-6P
854523-94-7P 854523-95-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 130346-59-7 130346-65-5 130347-67-0 130347-77-2
130347-78-3 130347-79-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 854523-79-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 854523-79-8 HCAPLUS

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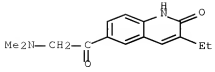

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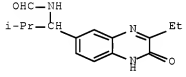
854523-82-3P 854523-83-4P 854523-86-7P
854523-87-8P 854523-88-9P 854523-89-0P
854523-90-3P 854523-91-4P 854523-92-5P
854523-94-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 854523-77-6 HCAPLUS
CN Formamide, N-[1-(3-ethyl-1,2-dihydro-2-oxo-6-quinoxalinyl)-2-methylpropyl]- (CA INDEX NAME)



RN 854523-78-7 HCAPLUS
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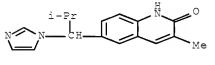

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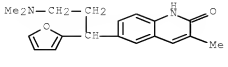
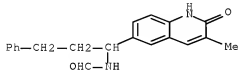
CN 2(1H)-Quinolinone, 6-[3-(dimethylamino)-1-(2-furanyl)propyl]-3-methyl- (CA INDEX NAME)



RN 854523-82-3 HCAPLUS
CN Formamide, N-[1-(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)-3-phenylpropyl]- (CA INDEX NAME)



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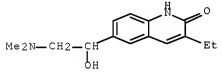
CN 2(1H)-Quinolinone, 6-[2-(dimethylamino)-1-hydroxyethyl]-3-ethyl- (CA INDEX NAME)



RN 854523-86-7 HCAPLUS
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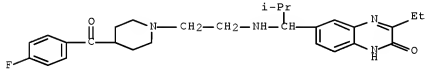

RN 854523-87-8 HCAPLUS
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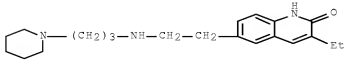
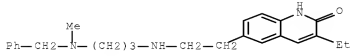
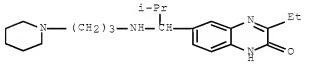


RN 854523-88-9 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[2-[[3-

[methyl(phenylmethyl)amino]propyl]amino]ethyl]- (CA INDEX NAME)



RN 854523-89-0 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[2-methyl-1-[[3-(1-piperidinyl)propyl]amino]propyl]- (CA INDEX NAME)



RN 854523-90-3 HCAPLUS
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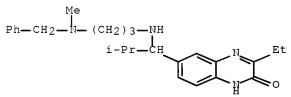

RN 854523-91-4 HCAPLUS
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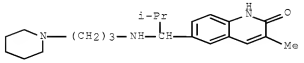

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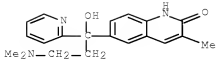

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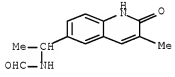
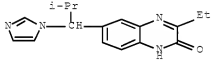


IT 130346-59-7 130346-65-5 130347-78-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)
RN 130346-59-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[1-(1H-imidazol-1-yl)-2-methylpropyl]- (CA INDEX NAME)



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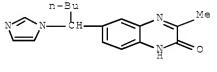

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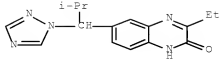

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:567163 HCAPLUS Full-text
DOCUMENT NUMBER: 143:78213
TITLE: Preparation of cyclohexylalkyl quinolinone and quinoxalinone derivatives as poly(ADP-ribose) polymerase (PARP) inhibitors
INVENTOR(S): Mabire, Dominique Jean-Pierre; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058843	A1	20050630	WO 2004-EP13165	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004299183	A1	20050630	AU 2004-299183	20041118
CA 2548273	A1	20050630	CA 2004-2548273	20041118
EP 1694653	A1	20060830	EP 2004-803192	20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
CN 1890225	A	20070103	CN 2004-80036656	20041118
BR 2004017571	A	20070320	BR 2004-17571	20041118
JP 2007513898	T	20070531	JP 2006-543409	20041118
MX 2006PA06573	A	20060731	MX 2006-PA6573	20060609
IN 2006DN03331	A	20070824	IN 2006-DN3331	20060609
KR 2006108753	A	20061018	KR 2006-713344	20060703
NO 2006003129	A	20060705	NO 2006-3129	20060705
PRIORITY APPLN. INFO.:			EP 2003-78918 A	20031210
			WO 2004-EP13165 W	20041118

OTHER SOURCE(S): CASREACT 143:78213; MARPAT 143:78213
ED Entered STN: 30 Jun 2005

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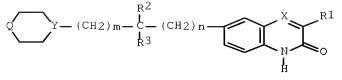

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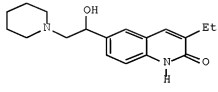

II

AB Title compds. I [n = 0-1; m = 0-1; X = N, CR4; Y = N, CH; Q = NH, O, CO, etc.; R1 = alkyl, thienyl; R2 = H or together with R3 may form O; R3 = H, alkyl, OH, etc. or R3 = (CH2)pZ; R4 = H or together with R1 may form (CH=CH)2; p = 0-2; Z = (un)substituted heterocycle] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of poly(ADP-ribose) polymerase (PARP). Thus, e.g., II was prepared by reaction of 3-ethyl-2(1H)-quinolinone with chloro-acetyl chloride followed by coupling with piperidine and subsequent reduction The inhibitory activity of I towards PARP-1 was evaluated in scintillation proximity assays and in filtration assays and it was revealed that compds. of the invention displayed inhibitory activity at initial test concns. of 10-6 and 10-5 M, resp. I as inhibitors of poly(ADP-ribose) polymerase should prove useful in the treatment of PARP-1 mediated disorders. Pharmaceutical compns. comprising I are disclosed.

IC ICM C07D241-44
ICS C07D401-06; A61K031-498; A61P043-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 855443-97-9P 855443-98-0P 855443-99-1P 855444-00-7P 855444-01-8P
855444-02-9P 855444-03-0P 855444-09-6P 855444-11-0P 855444-13-2P
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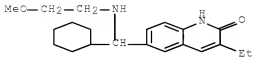
855444-47-2P 855444-50-7P 855444-52-9P 855444-54-1P 855444-56-3P
855444-58-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclohexylalkyl quinolinone and quinoxalinone derivs. as poly(ADP-ribose) polymerase (PARP) inhibitors)

IT 855444-20-1P 855444-33-6P 855444-40-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclohexylalkyl quinolinone and quinoxalinone derivs. as poly(ADP-ribose) polymerase (PARP) inhibitors)

RN 855444-20-1 HCAPLUS

CN 2(1H)-Quinolinone, 6-[cyclohexyl[(2-methoxyethyl)amino]methyl]-3-ethyl- (CA INDEX NAME)



RN 855444-33-6 HCAPLUS
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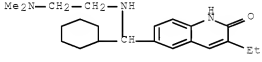

RN 855444-40-5 HCAPLUS
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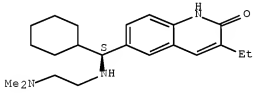
Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

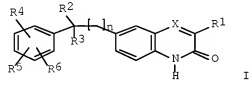
L89 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:523424 HCAPLUS Full-text
DOCUMENT NUMBER: 143:60001
TITLE: Preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors
INVENTOR(S): Mabire, Dominique Jean-pierre; Guillemont, Jerome Emile Georges; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054201	A1	20050616	WO 2004-EP13163	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295058	A1	20050616	AU 2004-295058	20041118
CA 2546300	A1	20050616	CA 2004-2546300	20041118
EP 1687277	A1	20060809	EP 2004-819601	20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1882547	A	20061220	CN 2004-80034176	20041118
BR 2004016206	A	20061226	BR 2004-16206	20041118
JP 2007511574	T	20070510	JP 2006-540338	20041118
US 20070072842	A1	20070329	US 2006-595891	20060518
IN 2006DN02813	A	20070803	IN 2006-DN2813	20060518
MX 2006PA05687	A	20060817	MX 2006-PA5687	20060519
KR 2006115393	A	20061108	KR 2006-710201	20060525
NO 2006002894	A	20060809	NO 2006-2894	20060620

PRIORITY APPLN. INFO.: WO 2003-EP13028 A 20031120
EP 2003-78860 A 20031205
WO 2003-EP130 A 20031120
WO 2004-EP13163 W 20041118

OTHER SOURCE(S): CASREACT 143:60001; MARPAT 143:60001
ED Entered STN: 17 Jun 2005
GI



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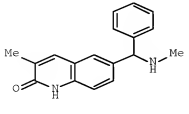

II

AB The title compds. I [n = 0-2; X = N, CR7; R7 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thiophenyl; R2 = H, OH, alkyl, alkynyl or taken together with R3 may form O; R3 = OH, OR10, SR11, etc.; R10, R11 = CHO, alkyl, (alkyl)amino, etc.; R4-R6 = H, halo, trihalomethyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from bromobenzene and 3-methyl-6-quinolinecarboxaldehyde, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IC ICM C07D215-227
ICS C07D241-44; C07D401-06; C07D403-06; C07D405-06; C07D405-14; C07D407-06; C07D407-12; A61K031-4704; A61K031-498; A61P001-04; A61P013-12; A61P019-02; A61P021-00; A61P025-28

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 854532-59-5P 854532-61-9P 854533-52-1P 854533-95-2P
854534-00-2P 854534-03-5P 854534-17-1P 854534-18-2P 854534-19-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 130346-68-8P 130346-69-9P 854532-58-4P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

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854534-79-5P 854534-80-8P 854534-81-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

IT 854532-61-9P 854533-95-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

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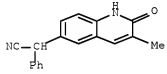
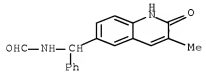


RN 854533-95-2 HCAPLUS
CN Formamide, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)phenylmethyl]- (CA INDEX NAME)



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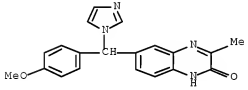
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 130346-68-8 HCAPLUS

CN 2(1H)-Quinoxalinone, 6-[1H-imidazol-1-yl(4-methoxyphenyl)methyl]-3-methyl- (CA INDEX NAME)



RN 130346-69-9 HCAPLUS

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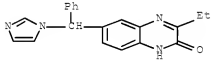

RN 854532-58-4 HCAPLUS

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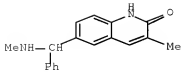

RN 854532-62-0 HCAPLUS
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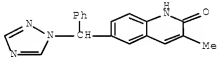

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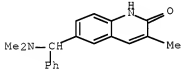
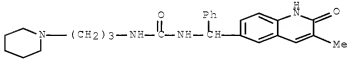
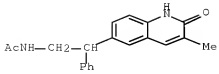


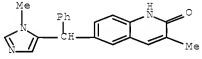
RN 854532-64-2 HCAPLUS
CN Urea, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)phenylmethyl]-N'-[3-(1-piperidinyl)propyl]- (CA INDEX NAME)



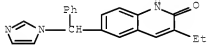
RN 854532-65-3 HCAPLUS
CN Acetamide, N-[2-(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)-2-phenylethyl]- (CA INDEX NAME)



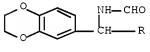
RN 854532-67-5 HCAPLUS
CN 2(1H)-Quinolinone, 3-methyl-6-[(1-methyl-1H-imidazol-5-yl)phenylmethyl]- (CA INDEX NAME)

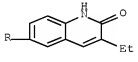


RN 854532-74-4 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-(1H-imidazol-1-ylphenylmethyl)- (CA INDEX NAME)

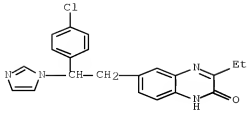


RN 854532-75-5 HCAPLUS
CN Formamide, N-[(2,3-dihydro-1,4-benzodioxin-6-yl)(3-ethyl-1,2-dihydro-2-oxo-6-quinolinyl)methyl]- (CA INDEX NAME)

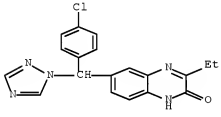




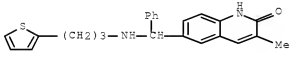
RN 854532-77-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[2-(4-chlorophenyl)-2-(1H-imidazol-1-yl)ethyl]-3-ethyl- (CA INDEX NAME)



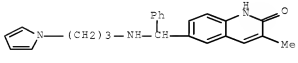
RN 854532-79-9 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(4-chlorophenyl)-1H-1,2,4-triazol-1-ylmethyl]-3-ethyl- (CA INDEX NAME)



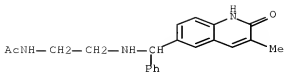
RN 854532-80-2 HCAPLUS
CN 2(1H)-Quinolinone, 3-methyl-6-[phenyl[[3-(2-thienyl)propyl]amino]methyl]- (CA INDEX NAME)



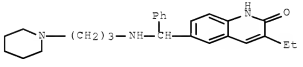
RN 854532-81-3 HCAPLUS
CN 2(1H)-Quinolinone, 3-methyl-6-[phenyl[[3-(1H-pyrrol-1-yl)propyl]amino]methyl]- (CA INDEX NAME)



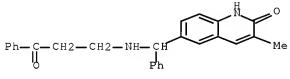
RN 854532-82-4 HCAPLUS
CN Acetamide, N-[2-[[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)phenylmethyl]amino]ethyl]- (CA INDEX NAME)



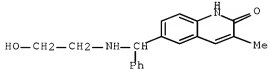
RN 854532-83-5 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[phenyl[[3-(1-piperidinyl)propyl]amino]methyl]- (CA INDEX NAME)



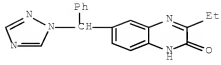
RN 854532-84-6 HCAPLUS
CN 2(1H)-Quinolinone, 3-methyl-6-[[(3-oxo-3-phenylpropyl)amino]phenylmethyl]- (CA INDEX NAME)



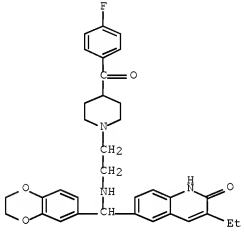
RN 854532-86-8 HCAPLUS
CN 2(1H)-Quinolinone, 6-[[(2-hydroxyethyl)amino]phenylmethyl]-3-methyl- (CA INDEX NAME)



RN 854532-87-9 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-(phenyl-1H-1,2,4-triazol-1-ylmethyl)- (CA INDEX NAME)



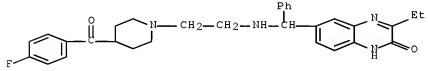
RN 854533-07-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(2,3-dihydro-1,4-benzodioxin-6-yl)[[2-[4-(4-fluorobenzoyl)-1-piperidinyl]ethyl]amino]methyl]-3-ethyl- (CA INDEX NAME)



RN 854533-14-5 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[[[2-[4-(4-fluorobenzoyl)-1-piperidinyl]ethyl]amino]phenylmethyl]-, ethanedioate (2:5) (CA INDEX NAME)

CM 1

CRN 854533-13-4
CMF C31 H33 F N4 O2



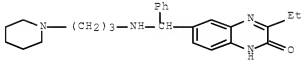
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-16-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[phenyl[[3-(1-piperidinyl)propyl]amino]methyl]-, ethanedioate (2:5) (CA INDEX NAME)

CM 1

CRN 854533-15-6
CMF C25 H32 N4 O



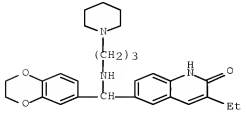
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-18-9 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(2,3-dihydro-1,4-benzodioxin-6-yl)[[3-(1-piperidinyl)propyl]amino]methyl]-3-ethyl-, ethanedioate (1:2) (CA INDEX NAME)

CM 1

CRN 854533-17-8
CMF C28 H35 N3 O3



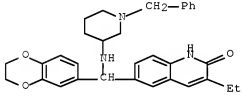
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-20-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(2,3-dihydro-1,4-benzodioxin-6-yl)[[1-(phenylmethyl)-3-piperidinyl]amino]methyl]-3-ethyl-, ethanedioate (2:5) (CA INDEX NAME)

CM 1

CRN 854533-19-0
CMF C32 H35 N3 O3



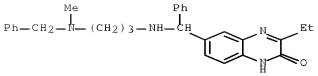
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-25-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[[[3-[methyl(phenylmethyl)amino]propyl]amino]phenylmethyl]-, ethanedioate (1:2) (CA INDEX NAME)

CM 1

CRN 854533-24-7
CMF C28 H32 N4 O



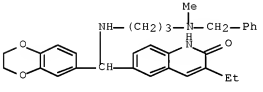
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-27-0 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(2,3-dihydro-1,4-benzodioxin-6-yl)[[3-[methyl(phenylmethyl)amino]propyl]amino]methyl]-3-ethyl-, ethanedioate (1:2) (CA INDEX NAME)

CM 1

CRN 854533-26-9
CMF C31 H35 N3 O3



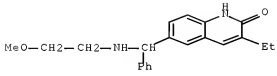
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 854533-29-2 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[[(2-methoxyethyl)amino]phenylmethyl]-, ethanedioate (1:2) (CA INDEX NAME)

CM 1

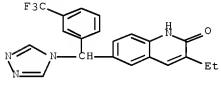
CRN 854533-28-1
CMF C21 H24 N2 O2



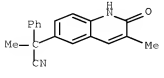
CM 2

CRN 144-62-7
CMF C2 H2 O4

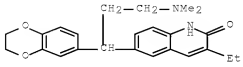
RN 854533-43-0 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[4H-1,2,4-triazol-4-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)



RN 854533-56-5 HCAPLUS
CN 6-Quinolineacetonitrile, 1,2-dihydro-α,3-dimethyl-2-oxo-α-phenyl- (CA INDEX NAME)



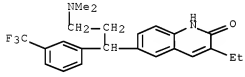
RN 854533-62-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-(dimethylamino)propyl]-3-ethyl- (CA INDEX NAME)



RN 854533-65-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-[3-(dimethylamino)-1-[3-(trifluoromethyl)phenyl]propyl]-3-ethyl-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

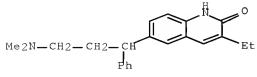
CRN 854533-64-5
CMF C23 H25 F3 N2 O



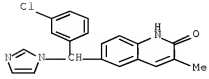
CM 2

CRN 144-62-7
CMF C2 H2 O4

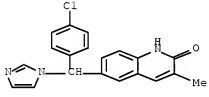
RN 854533-67-8 HCAPLUS
CN 2(1H)-Quinolinone, 6-[3-(dimethylamino)-1-phenylpropyl]-3-ethyl- (CA INDEX NAME)



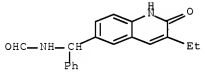
RN 854533-71-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



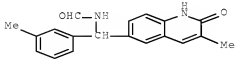
RN 854533-73-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



RN 854533-75-8 HCAPLUS
CN Formamide, N-[(3-ethyl-1,2-dihydro-2-oxo-6-quinolinyl)phenylmethyl]- (CA INDEX NAME)

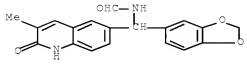


RN 854533-79-2 HCAPLUS
CN Formamide, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)(3-methylphenyl)methyl]- (CA INDEX NAME)

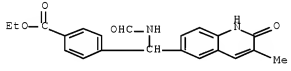


RN 854533-81-6 HCAPLUS

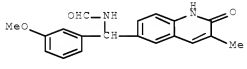
CN Formamide, N-[1,3-benzodioxol-5-yl(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)methyl]- (CA INDEX NAME)



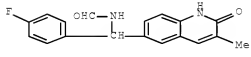
RN 854533-83-8 HCAPLUS
CN Benzoic acid, 4-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)(formylamino)methyl]-, ethyl ester (CA INDEX NAME)



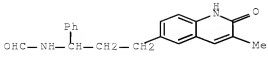
RN 854533-85-0 HCAPLUS
CN Formamide, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)(3-methoxyphenyl)methyl]- (CA INDEX NAME)



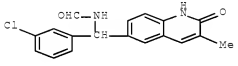
RN 854533-87-2 HCAPLUS
CN Formamide, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)(4-fluorophenyl)methyl]- (CA INDEX NAME)



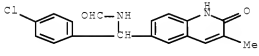
RN 854533-89-4 HCAPLUS
CN Formamide, N-[3-(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)-1-phenylpropyl]- (CA INDEX NAME)



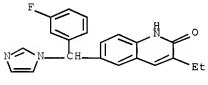
RN 854533-91-8 HCAPLUS
CN Formamide, N-[(3-chlorophenyl)(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)methyl]- (CA INDEX NAME)



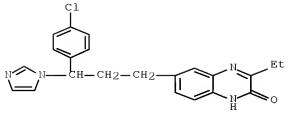
RN 854533-93-0 HCAPLUS
CN Formamide, N-[(4-chlorophenyl)(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)methyl]- (CA INDEX NAME)



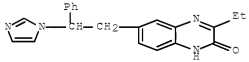
RN 854534-05-7 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[(3-fluorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



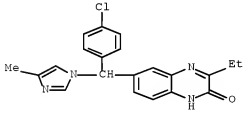
RN 854534-08-0 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[3-(4-chlorophenyl)-3-(1H-imidazol-1-yl)propyl]-3-ethyl- (CA INDEX NAME)



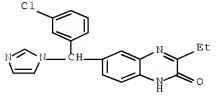
RN 854534-09-1 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[2-(1H-imidazol-1-yl)-2-phenylethyl]- (CA INDEX NAME)



RN 854534-12-6 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(4-chlorophenyl)(4-methyl-1H-imidazol-1-yl)methyl]-3-ethyl- (CA INDEX NAME)

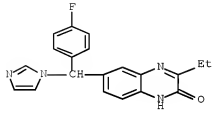


RN 854534-13-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-ethyl- (CA INDEX NAME)

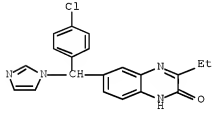


RN 854534-15-9 HCAPLUS

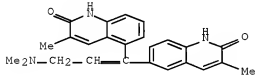
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[(4-fluorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



RN 854534-16-0 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-ethyl- (CA INDEX NAME)

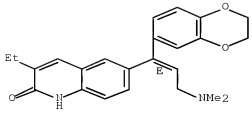


RN 854534-23-9 HCAPLUS
CN 2(1H)-Quinolinone, 5-[1-(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)-3-(dimethylamino)-1-propen-1-yl]-3-methyl- (CA INDEX NAME)



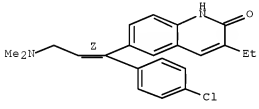
RN 854534-24-0 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(1E)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-(dimethylamino)-1-propen-1-yl]-3-ethyl- (CA INDEX NAME)

Double bond geometry as shown.



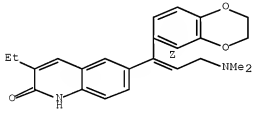
RN 854534-25-1 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(1Z)-1-(4-chlorophenyl)-3-(dimethylamino)-1-propen-1-yl]-3-ethyl- (CA INDEX NAME)

Double bond geometry as shown.



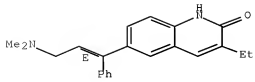
RN 854534-26-2 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(1Z)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-(dimethylamino)-1-propen-1-yl]-3-ethyl- (CA INDEX NAME)

Double bond geometry as shown.



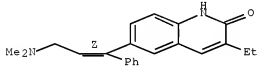
RN 854534-27-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(1E)-3-(dimethylamino)-1-phenyl-1-propen-1-yl]-3-ethyl- (CA INDEX NAME)

Double bond geometry as shown.

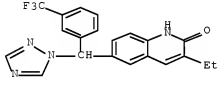


RN 854534-28-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(1Z)-3-(dimethylamino)-1-phenyl-1-propen-1-yl]-3-ethyl- (CA INDEX NAME)

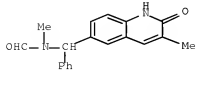
Double bond geometry as shown.



RN 854535-35-6 HCAPLUS
CN 2(1H)-Quinolinone, 3-ethyl-6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)



IT 854534-38-6P 854534-48-8P 854534-49-9P
854534-50-2P 854534-51-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)
RN 854534-38-6 HCAPLUS
CN Formamide, N-[(1,2-dihydro-3-methyl-2-oxo-6-quinolinyl)phenylmethyl]-N-methyl- (CA INDEX NAME)



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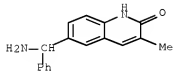
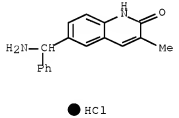
CN 2(1H)-Quinolinone, 6-(aminophenylmethyl)-3-methyl- (CA INDEX NAME)



RN 854534-49-9 HCAPLUS
CN 2(1H)-Quinolinone, 6-(aminophenylmethyl)-3-methyl-, hydrochloride (1:1)
(CA INDEX NAME)



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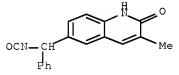
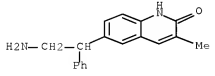
CN 2(1H)-Quinolinone, 6-(isocyanatophenylmethyl)-3-methyl- (CA INDEX NAME)



RN 854534-51-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-(2-amino-1-phenylethyl)-3-methyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L89 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:388171 HCAPLUS Full-text
DOCUMENT NUMBER: 131:44827
TITLE: Preparation of N-[(imidazolyl- and triazolylalkyl)phenyl]acetamides and analogs as retinoid metabolism inhibitors
INVENTOR(S): Mabire, Dominique; Adelinet, Christophe Denis; Csoka, Imre Christian; Venet, Marc Gaston
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929674	A1	19990617	WO 1998-EP8126	19981208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2312720	A1	19990617	CA 1998-2312720	19981208
AU 9921608	A	19990628	AU 1999-21608	19981208
EP 1037880	A1	20000927	EP 1998-965820	19981208
EP 1037880	B1	20040630		
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TR 200001645	T2	20001221	TR 2000-1645	19981208
HU 2001000860	A2	20010928	HU 2001-860	19981208
HU 2001000860	A3	20030328		
JP 2001524400	T	20011211	JP 2000-524271	19981208
AT 270277	T	20040715	AT 1998-965820	19981208
PT 1037880	T	20041130	PT 1998-965820	19981208
ES 2224462	T3	20050301	ES 1998-965820	19981208
TW 523503	B	20030311	TW 1998-87120384	19981209
ZA 9811351	A	20000612	ZA 1998-11351	19981210
US 6319939	B1	20011120	US 2000-555775	20000601
BG 104499	A	20010831	BG 2000-104499	20000602
US 20020115653	A1	20020822	US 2001-962551	20010925
US 6936626	B2	20050830		
US 20050165018	A1	20050728	US 2005-81393	20050316
US 7179825	B2	20070220		
US 20070105858	A1	20070510	US 2006-551045	20061019
US 20080058334	A1	20080306	US 2007-926699	20071029

PRIORITY APPLN. INFO.:
EP 1997-203886 A 19971211
WO 1998-EP8126 W 19981208
US 2000-555775 A3 20000601
US 2001-962551 A3 20010925
US 2005-81393 A3 20050316
US 2006-551045 A1 20061019

OTHER SOURCE(S): MARPAT 131:44827
ED Entered STN: 23 Jun 1999

AB R4C(:X)NR3ZCRR1R2 [I; R = pyrrolyl, imidazolyl, triazolyl, pyridinyl, etc.; R1 = H, OH, alkyl, aryl; R2 = H, (un)substituted alkyl, (hetero)aryl, etc.; R3 = H, (ar)alkyl, (hetero)aryl, etc.; R4 = H, OH, (un)substituted alkyl, alkoxy, etc.; X = O, S, NR3; Z = 1,4-phenylene] were prepared Thus, 4-(AcHN)C6H4CHRCHMe2 (II; R = OH) was O-mesylated and the product condensed with 1H-1,2,4-triazole to give II (R = 1H-1,2,4-triazol-1-yl). Data for biol. activity of I were given.

IC ICM C07D233-56
ICS C07D249-08; C07D213-40; C07D401-12; C07D403-12; C07D405-12; C07D409-12; C07D417-12

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 227282-09-9P 227282-10-2P 227282-11-3P 227282-12-4P 227282-13-5P
227282-14-6P 227282-15-7P 227282-16-8P 227282-17-9P 227282-18-0P
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227284-50-6P 227284-51-7P 227284-52-8P 227284-53-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

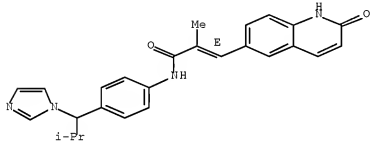
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-[(imidazolyl- and triazolylalkyl)phenyl]acetamides and analogs as retinoid metabolism inhibitors)

IT 227284-26-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-[(imidazolyl- and triazolylalkyl)phenyl]acetamides and analogs as retinoid metabolism inhibitors)

RN 227284-26-6 HCAPLUS

CN 2-Propenamide, 3-(1,2-dihydro-2-oxo-6-quinolinyl)-N-[4-[1-(1H-imidazol-1-yl)-2-methylpropyl]phenyl]-2-methyl-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:527663 HCAPLUS Full-text
DOCUMENT NUMBER: 125:167994
ORIGINAL REFERENCE NO.: 125:31485a,31488a
TITLE: Preparation of 6-[triazolyl(3-trifluoromethylphenyl)methyl]-2-quinolin(thi)ones for treatment of keratinization disorders
INVENTOR(S): Venet, Marc Gaston; Mabire, Dominique Jean-Pierre; Sanz, Gerard Charles
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620200	A1	19960704	WO 1995-EP5173	19951221

W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,

NE, SN, TD, TG

IN	1995CA01685	A	20050304	IN 1995-CA1685	19951220
CA	2207268	A1	19960704	CA 1995-2207268	19951221
AU	9644362	A	19960719	AU 1996-44362	19951221
AU	698199	B2	19981029		
EP	800524	A1	19971015	EP 1995-943237	19951221
EP	800524	B1	20011031		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE

CN	1171789	A	19980128	CN 1995-197162	19951221
CN	1085668	C	20020529		
JP	10511654	T	19981110	JP 1995-520222	19951221
BR	9510504	A	19990601	BR 1995-10504	19951221
RU	2165419	C2	20010420	RU 1997-112898	19951221
AT	207924	T	20011115	AT 1995-943237	19951221
PT	800524	T	20020429	PT 1995-943237	19951221
ES	2166838	T3	20020501	ES 1995-943237	19951221
PL	182956	B1	20020531	PL 1995-321041	19951221
ZA	9510989	A	19970627	ZA 1995-10989	19951227
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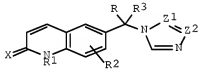
US	5922734	A	19990713	US 1997-860239	19970616
FI	9702794	A	19970627	FI 1997-2794	19970627
NO	9703029	A	19970627	NO 1997-3029	19970627
NO	311220	B1	20011029		

PRIORITY APPLN. INFO.:				EP 1994-203773	A 19941228
				WO 1995-EP5173	W 19951221

OTHER SOURCE(S): MARPAT 125:167994

ED Entered STN: 03 Sep 1996

GI



I

AB Title compds. [I; R = 3-(F3C)C6H4][II; R1 = H, NH2, alkyl; R2,R3 = H, halo, alkyl; X = O or S; 1 of Z1,Z2 = N and the other = CH] were prepared Thus, (R)-II (R1-R3 = H, X = O, Z1 = N, Z2 = CH) gave complete suppression of estradiol undecylate-induced vaginal keratinization in 50% of ovariectomized rats at 1.25mg/kg orally.

IC ICM C07D521-00
ICS C07D401-06; A61K031-47

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 180421-65-2P 180421-66-3P 180421-67-4P
180421-68-5P 180421-69-6P 180421-70-9P
180421-71-0P 180421-72-1P 180421-73-2P
180421-74-3P 180421-75-4P 180421-76-5P
180421-77-6P 180421-78-7P 180421-79-8P
180421-80-1P 180421-81-2P 180421-82-3P
180421-83-4P 180421-84-5P 180421-85-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-[triazolyl(3-trifluoromethylphenyl)methyl]-2-

quinolin(thi)ones for treatment of keratinization disorders)

IT 180421-65-2P 180421-66-3P 180421-67-4P
180421-68-5P 180421-70-9P 180421-71-0P
180421-72-1P 180421-73-2P 180421-74-3P
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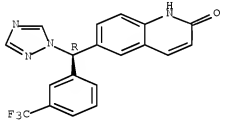
180421-82-3P 180421-85-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-[triazolyl(3-trifluoromethylphenyl)methyl]-2-quinolin(thi)ones for treatment of keratinization disorders)

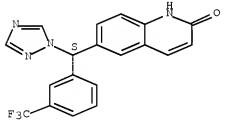
RN 180421-65-2 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

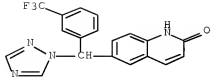


RN 180421-66-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

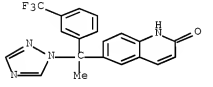
Absolute stereochemistry. Rotation (+).



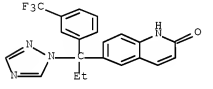
RN 180421-67-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)



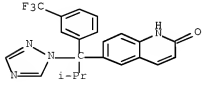
RN 180421-68-5 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]ethyl]- (CA INDEX NAME)



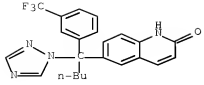
RN 180421-70-9 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]propyl]- (CA INDEX NAME)



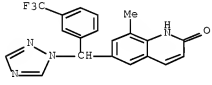
RN 180421-71-0 HCAPLUS
CN 2(1H)-Quinolinone, 6-[2-methyl-1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]propyl]- (CA INDEX NAME)



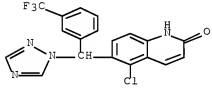
RN 180421-72-1 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]pentyl]- (CA INDEX NAME)



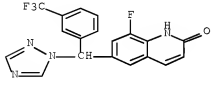
RN 180421-73-2 HCAPLUS
CN 2(1H)-Quinolinone, 8-methyl-6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)



RN 180421-74-3 HCAPLUS
CN 2(1H)-Quinolinone, 5-chloro-6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

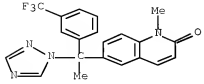


RN 180421-75-4 HCAPLUS
CN 2(1H)-Quinolinone, 8-fluoro-6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

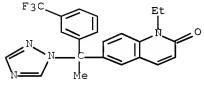


RN 180421-77-6 HCAPLUS

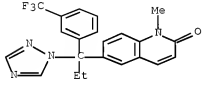
CN 2(1H)-Quinolinone, 1-methyl-6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]ethyl]- (CA INDEX NAME)



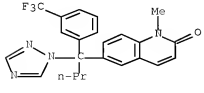
RN 180421-78-7 HCAPLUS
CN 2(1H)-Quinolinone, 1-ethyl-6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]ethyl]- (CA INDEX NAME)



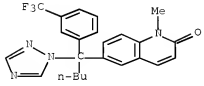
RN 180421-79-8 HCAPLUS
CN 2(1H)-Quinolinone, 1-methyl-6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]propyl]- (CA INDEX NAME)



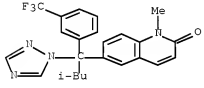
RN 180421-80-1 HCAPLUS
CN 2(1H)-Quinolinone, 1-methyl-6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]butyl]- (CA INDEX NAME)



RN 180421-81-2 HCAPLUS
CN 2(1H)-Quinolinone, 1-methyl-6-[1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]pentyl]- (CA INDEX NAME)

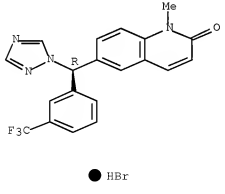


RN 180421-82-3 HCAPLUS
CN 2(1H)-Quinolinone, 1-methyl-6-[3-methyl-1-(1H-1,2,4-triazol-1-yl)-1-[3-(trifluoromethyl)phenyl]butyl]- (CA INDEX NAME)



RN 180421-85-6 HCAPLUS
CN 2(1H)-Quinolinone, 1-methyl-6-[1H-1,2,4-triazol-1-yl[3-(trifluoromethyl)phenyl]methyl]-, monohydrobromide, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1990:612014 HCAPLUS Full-text
DOCUMENT NUMBER: 113:212014

ORIGINAL REFERENCE NO.: 113:35835a,35838a
TITLE: Preparation of (1H-azol-1-ylmethyl)quinolines, -quinazolines, and -quinoxalines as drugs
INVENTOR(S): Freyne, Eddy Jean Edgard; Venet, Marc Gaston; Raeymaekers, Alfons Herman Margaretha; Sanz, Gerard Charles
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 106 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 371564	A2	19900606	EP 1989-203014	19891128
EP 371564	A3	19910529		
EP 371564	B1	19950712		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5028606	A	19910702	US 1989-434957	19891113
US 5037829	A	19910806	US 1989-435120	19891113
CA 2002864	A1	19900529	CA 1989-2002864	19891114
CA 2002864	C	19991116		
DK 8905994	A	19900530	DK 1989-5994	19891128
DK 172748	B1	19990628		
NO 8904734	A	19900530	NO 1989-4734	19891128
NO 174509	B	19940207		
NO 174509	C	19940518		
AU 8945646	A	19900607	AU 1989-45646	19891128
AU 620946	B2	19920227		
HU 52498	A2	19900728	HU 1989-6220	19891128
HU 205106	B	19920330		
ZA 8909076	A	19910731	ZA 1989-9076	19891128
SU 1780536	A3	19921207	SU 1989-4742543	19891128
IL 92486	A	19930708	IL 1989-92486	19891128
ES 2088889	T3	19961001	ES 1989-203014	19891128
FI 101964	B	19980930	FI 1989-5687	19891128
FI 101964	B1	19980930		
CN 1042912	A	19900613	CN 1989-108925	19891129
CN 1033752	C	19970108		
JP 02223579	A	19900905	JP 1989-307793	19891129
JP 2916181	B2	19990705		
US 5151421	A	19920929	US 1991-672298	19910320
US 5185346	A	19930209	US 1991-704746	19910523
US 5268380	A	19931207	US 1992-973871	19921110
US 5441954	A	19950815	US 1993-131817	19931005
CN 1106004	A	19950802	CN 1994-117801	19941102
CN 1036002	C	19971001		
CN 1106005	A	19950802	CN 1994-117802	19941102
CN 1036003	C	19971001		
US 5612354	A	19970318	US 1995-409551	19950323

PRIORITY APPLN. INFO.:

GB 1988-27820	A	19881129
GB 1988-27821	A	19881129
GB 1988-27822	A	19881129
US 1989-434205	B2	19891113
US 1989-434957	A3	19891113
US 1991-704746	A3	19910523
US 1992-973871	A3	19921110
US 1993-131817	A3	19931005

OTHER SOURCE(S): MARPAT 113:212014
ED Entered STN: 08 Dec 1990
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; R = H, alkyl; X1:X2 = CH:CH, CH:N, N:CH; Y = H, alkyl, cycloalkyl, alkenyl, alkynyl, (un)substituted aryl, aralkyl; Z = (un)substituted (oxo)quinolinyl, (oxo- or thioxo)quinazolinyl, (oxo- or dioxo)quinoxalinyl] were prepared as retinoic acid metabolism inhibitors, aromatase inhibitors, etc. Thus, 3,4-dihydroquinolin-2(1H)-one was stirred 2 h at 70° with BzCl in DMF containing AlCl3 and the product reduced by NaBH4 to give hydroxymethylquinolinone II (R1 = Ph, R2 = OH). II (R1 = Me, R2 = OH) was stirred overnight with SOCl2 in THF and the product II (R1 = Me, R2 = Cl) stirred overnight at 60-70° with 1H-imidazole in DMSO to give II (R1 = Me, R2 = imidazolo) which maintained plasma levels of i.v. administered all-trans-retinoic acid at ≥10 ng/mL in rats 2 h after oral administration of 40 mg/kg.
IC ICM C07D401-06
ICS C07D403-06; C07D403-14; C07D409-14; C07D401-14; A61K031-47; A61K031-495; C07D215-12; C07D233-60; C07D249-08; C07D239-88
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 120067-40-5P 120067-41-6P 120067-51-8P 130140-41-9P
130343-93-0P 130343-94-1P 130343-95-2P
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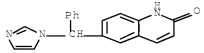
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as retinoate metabolism and aromatase inhibitor)

IT 130347-37-4P 130347-38-5P 130347-39-6P 130347-40-9P
130347-41-0P 130347-42-1P 130347-43-2P 130347-44-3P
130347-45-4P 130347-46-5P 130347-47-6P
130347-48-7P 130347-49-8P 130347-50-1P 130347-51-2P 130347-52-3P
130347-53-4P 130347-54-5P 130347-55-6P 130347-56-7P 130347-57-8P
130347-58-9P 130347-59-0P 130347-60-3P 130347-61-4P 130347-62-5P
130347-63-6P 130347-64-7P 130347-65-8P 130347-66-9P 130347-67-0P
130347-68-1P 130347-69-2P 130347-70-5P 130347-71-6P 130347-72-7P
130347-73-8P 130347-74-9P 130347-75-0P 130347-76-1P 130347-77-2P
130347-78-3P 130347-79-4P 130347-80-7P 130347-81-8P
130347-82-9P 130347-83-0P 130347-84-1P 130347-85-2P 130347-86-3P
130347-87-4P 130347-88-5P 130347-89-6P 130347-90-9P 130347-91-0P
130347-92-1P 130347-93-2P 130347-94-3P 130347-95-4P 130347-96-5P
130347-97-6P 130347-98-7P 130347-99-8P 130368-35-3P
130368-36-4P 130368-37-5P 130368-38-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as retinoate metabolism and aromatase inhibitor)

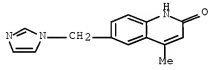
IT 120067-41-6P 130343-93-0P 130343-94-1P
130343-95-2P 130343-96-3P 130343-97-4P
130343-98-5P 130343-99-6P 130344-00-2P
130344-01-3P 130344-02-4P 130344-03-5P
130344-04-6P 130344-05-7P 130346-18-8P
130346-22-4P 130346-23-5P 130346-25-7P
130346-26-8P 130346-27-9P 130346-29-1P
130346-30-4P 130346-32-6P 130346-33-7P
130346-34-8P 130346-42-8P 130346-48-4P
130346-49-5P 130346-52-0P 130346-53-1P
130346-55-3P 130346-56-4P 130346-58-6P
130346-59-7P 130346-63-3P 130346-65-5P
130346-66-6P 130346-68-8P 130346-69-9P
130346-72-4P 130346-77-9P 130346-85-9P
130346-90-6P 130346-98-4P 130347-00-1P
130347-01-2P 130347-23-8P 130347-26-1P
130347-28-3P 130347-30-7P 130347-31-8P
130347-32-9P 130347-33-0P 130347-34-1P
130347-36-3P 130347-37-4P 130347-39-6P
130347-41-0P 130347-43-2P 130347-45-4P
130347-46-5P 130347-47-6P 130347-78-3P
130368-36-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as retinoate metabolism and aromatase inhibitor)

RN 120067-41-6 HCAPLUS

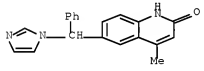
CN 2(1H)-Quinolinone, 6-(1H-imidazol-1-ylphenylmethyl)- (CA INDEX NAME)



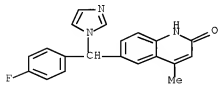
RN 130343-93-0 HCAPLUS
CN 2(1H)-Quinolinone, 6-(1H-imidazol-1-ylmethyl)-4-methyl- (CA INDEX NAME)



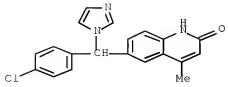
RN 130343-94-1 HCAPLUS
CN 2(1H)-Quinolinone, 6-(1H-imidazol-1-ylphenylmethyl)-4-methyl- (CA INDEX NAME)



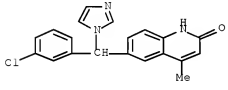
RN 130343-95-2 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(4-fluorophenyl)-1H-imidazol-1-ylmethyl]-4-methyl- (CA INDEX NAME)



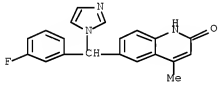
RN 130343-96-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-4-methyl- (CA INDEX NAME)



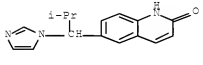
RN 130343-97-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]-4-methyl- (CA INDEX NAME)



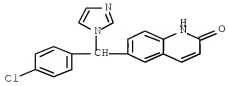
RN 130343-98-5 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(3-fluorophenyl)-1H-imidazol-1-ylmethyl]-4-methyl- (CA INDEX NAME)



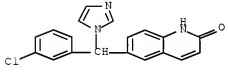
RN 130343-99-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]- (CA INDEX NAME)



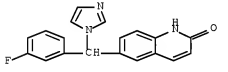
RN 130344-00-2 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



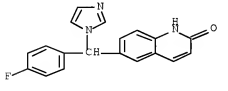
RN 130344-01-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



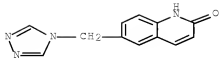
RN 130344-02-4 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(3-fluorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



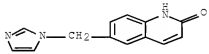
RN 130344-03-5 HCAPLUS
CN 2(1H)-Quinolinone, 6-[(4-fluorophenyl)-1H-imidazol-1-ylmethyl]- (CA INDEX NAME)



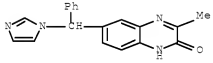
RN 130344-04-6 HCAPLUS
CN 2(1H)-Quinolinone, 6-(4H-1,2,4-triazol-4-ylmethyl)- (CA INDEX NAME)



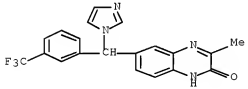
RN 130344-05-7 HCAPLUS
CN 2(1H)-Quinolinone, 6-(1H-imidazol-1-ylmethyl)- (CA INDEX NAME)



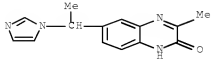
RN 130346-18-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(1H-imidazol-1-ylphenylmethyl)-3-methyl- (CA INDEX NAME)



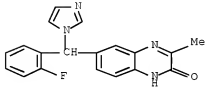
RN 130346-22-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1H-imidazol-1-yl[3-(trifluoromethyl)phenyl]methyl]-3-methyl- (CA INDEX NAME)



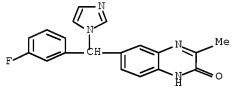
RN 130346-23-5 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)ethyl]-3-methyl- (CA INDEX NAME)



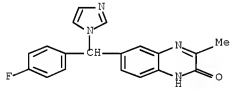
RN 130346-25-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(2-fluorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



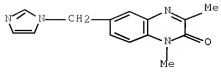
RN 130346-26-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(3-fluorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



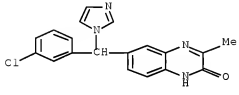
RN 130346-27-9 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(4-fluorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



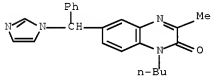
RN 130346-29-1 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(1H-imidazol-1-ylmethyl)-1,3-dimethyl- (CA INDEX NAME)



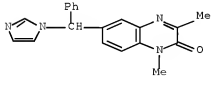
RN 130346-30-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)



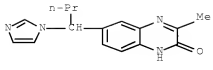
RN 130346-32-6 HCAPLUS
CN 2(1H)-Quinoxalinone, 1-butyl-6-(1H-imidazol-1-ylphenylmethyl)-3-methyl- (CA INDEX NAME)



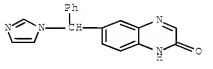
RN 130346-33-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(1H-imidazol-1-ylphenylmethyl)-1,3-dimethyl- (CA INDEX NAME)



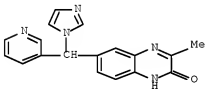
RN 130346-34-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)butyl]-3-methyl- (CA INDEX NAME)



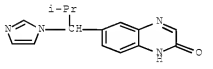
RN 130346-42-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(1H-imidazol-1-ylphenylmethyl)- (CA INDEX NAME)



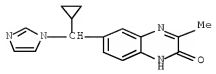
RN 130346-48-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(1H-imidazol-1-yl-3-pyridinylmethyl)-3-methyl- (CA INDEX NAME)



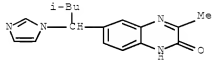
RN 130346-49-5 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]- (CA INDEX NAME)



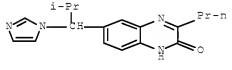
RN 130346-52-0 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(cyclopropyl-1H-imidazol-1-ylmethyl)-3-methyl- (CA INDEX NAME)



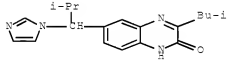
RN 130346-53-1 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-3-methylbutyl]-3-methyl- (CA INDEX NAME)



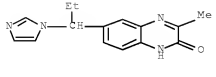
RN 130346-55-3 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]-3-propyl- (CA INDEX NAME)



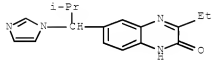
RN 130346-56-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]-3-(2-methylpropyl)- (CA INDEX NAME)



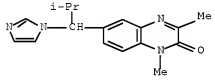
RN 130346-58-6 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)propyl]-3-methyl- (CA INDEX NAME)



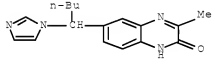
RN 130346-59-7 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-[1-(1H-imidazol-1-yl)-2-methylpropyl]- (CA INDEX NAME)



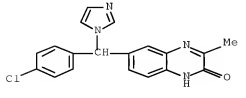
RN 130346-63-3 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]-1,3-dimethyl- (CA INDEX NAME)



RN 130346-65-5 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)pentyl]-3-methyl- (CA INDEX NAME)

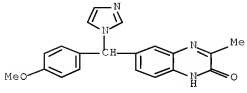


RN 130346-66-6 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-methyl- (CA INDEX NAME)

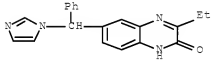


RN 130346-68-8 HCAPLUS

CN 2(1H)-Quinoxalinone, 6-[1H-imidazol-1-yl(4-methoxyphenyl)methyl]-3-methyl- (CA INDEX NAME)



RN 130346-69-9 HCAPLUS
CN 2(1H)-Quinoxalinone, 3-ethyl-6-(1H-imidazol-1-ylphenylmethyl)- (CA INDEX NAME)



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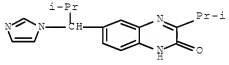
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)-2-methylpropyl]-3-(1-methylethyl)- (CA INDEX NAME)



RN 130346-77-9 HCAPLUS
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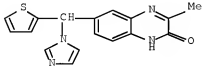

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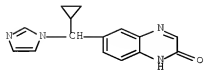

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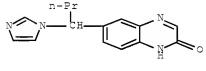
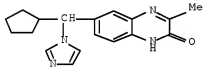
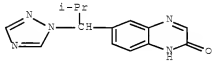
CN 2(1H)-Quinoxalinone, 6-[1-(1H-imidazol-1-yl)butyl]- (CA INDEX NAME)



RN 130346-98-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(cyclopentyl-1H-imidazol-1-ylmethyl)-3-methyl- (CA INDEX NAME)



RN 130347-00-1 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[2-methyl-1-(1H-1,2,4-triazol-1-yl)propyl]- (CA INDEX NAME)



RN 130347-01-2 HCAPLUS
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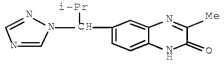
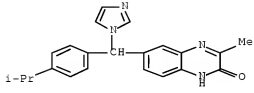


RN 130347-23-8 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[1H-imidazol-1-yl[4-(1-methylethyl)phenyl]methyl]-3-methyl- (CA INDEX NAME)



RN 130347-26-1 HCAPLUS
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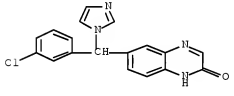
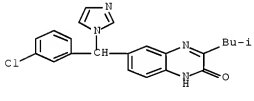


RN 130347-28-3 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-[(3-chlorophenyl)-1H-imidazol-1-ylmethyl]-3-(2-methylpropyl)- (CA INDEX NAME)



RN 130347-30-7 HCAPLUS
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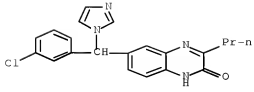

RN 130347-31-8 HCAPLUS
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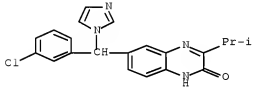

RN 130347-32-9 HCAPLUS
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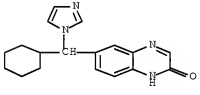

RN 130347-33-0 HCAPLUS
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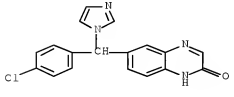

RN 130347-34-1 HCAPLUS
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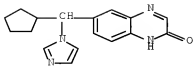

RN 130347-36-3 HCAPLUS
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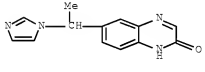

RN 130347-37-4 HCAPLUS
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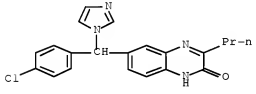

RN 130347-39-6 HCAPLUS
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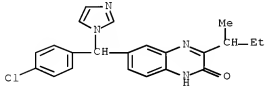

RN 130347-41-0 HCAPLUS
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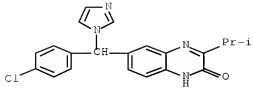

RN 130347-43-2 HCAPLUS
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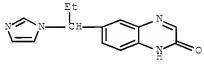

RN 130347-45-4 HCAPLUS
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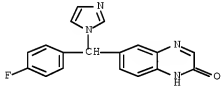

RN 130347-46-5 HCAPLUS
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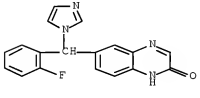

RN 130347-47-6 HCAPLUS
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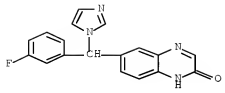

RN 130347-78-3 HCAPLUS
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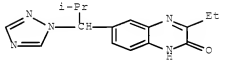
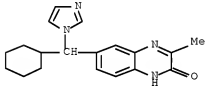
(CA INDEX NAME)



RN 130368-36-4 HCAPLUS
CN 2(1H)-Quinoxalinone, 6-(cyclohexyl-1H-imidazol-1-ylmethyl)-3-methyl- (CA
INDEX NAME)



=> d iall abeq tech abex hitstr 7-8
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, BIOTECHDS' - CONTINUE? (Y)/N:y

L89 ANSWER 7 OF 9 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2001-582115 [65] WPIX
DOC. NO. CPI: C2001-172609 [65]
TITLE: Use of a combination of a nitrogen mustard or nitrosourea alkylating agent and a farnesyl protein transferase inhibitor for inhibiting growth of tumor cells and treating cancer
DERWENT CLASS: B02
INVENTOR: RYBAK M E M; RYBAK M E M J P I
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV; (RYBA-I) RYBAK M E M
COUNTRY COUNT: 93

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001064217	A2	20010907	(200165)*	EN	41[0]	
AU 2001035496	A	20010912	(200204)	EN		
EP 1261348	A2	20021204	(200280)	EN		
US 20030078281	A1	20030424	(200330)	EN		
JP 2003525244	W	20030826	(200357)	JA	65	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001064217	A2	WO 2001-EP2168	20010226
AU 2001035496	A	AU 2001-35496	20010226
EP 1261348	A2	EP 2001-907564	20010226
JP 2003525244	W	JP 2001-563114	20010226
EP 1261348	A2	WO 2001-EP2168	20010226
US 20030078281	A1	WO 2001-EP2168	20010226
JP 2003525244	W	WO 2001-EP2168	20010226
US 20030078281	A1	US 2002-220220	20020828

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001035496	A Based on	WO 2001064217 A
EP 1261348	A2 Based on	WO 2001064217 A
JP 2003525244	W Based on	WO 2001064217 A

PRIORITY APPLN. INFO: EP 2000-200691 20000229

INT. PATENT CLASSIF.:

MAIN:	A61K031-4709
IPC RECLASSIF.:	A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-17 [I,A]; A61K0031-17 [I,A]; A61K0031-17 [I,C]; A61K0031-17 [I,C]; A61K0031-185 [I,C]; A61K0031-185 [I,C]; A61K0031-195 [I,A]; A61K0031-196 [I,A]; A61K0031-47 [I,A]; A61K0031-47 [I,C]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61K0031-519 [I,A]; A61K0031-519 [I,C]; A61K0031-675 [I,A]; A61K0031-675 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,C]; A61P0035-04 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]
ECLA:	A61K0031-47+M; A61K0031-675+M
USCLASS NCLM:	514/312.000
NCLS:	514/314.000; 514/589.000

JAP. PATENT CLASSIF.:

MAIN/SEC.:	A61K0031-165; A61K0031-17; A61K0031-196; A61K0031-4709; A61K0031-519; A61K0045-00; A61P0035-04; A61P0043-00 111
FTERM CLASSIF.:	4C084; 4C086; 4C201; 4C206; 4C086/AA01; 4C206/AA01; 4C084/AA02; 4C086/AA02; 4C206/AA02; 4C084/AA03; 4C084/AA19; 4C084/BA44; 4C086/BC38; 4C086/CB05; 4C086/DA35; 4C206/FA31; 4C086/GA07; 4C086/GA08; 4C206/HA26; 4C084/MA02; 4C086/MA02; 4C206/MA02; 4C086/MA04; 4C206/MA04; 4C206/MA14; 4C084/MA17; 4C086/MA17; 4C206/MA17; 4C084/MA22; 4C086/MA22; 4C084/MA23; 4C086/MA23; 4C206/MA24; 4C084/MA28; 4C086/MA28; 4C084/MA31; 4C086/MA31; 4C084/MA32; 4C086/MA32; 4C084/MA35; 4C086/MA35; 4C084/MA36; 4C086/MA36; 4C084/MA37; 4C086/MA37; 4C206/MA37;

4C084/MA41; 4C086/MA41; 4C206/MA42; 4C084/MA43; 4C086/MA43; 4C206/MA43; 4C206/MA48; 4C206/MA51; 4C084/MA52; 4C086/MA52; 4C206/MA52; 4C206/MA55; 4C206/MA56; 4C206/MA57; 4C084/MA60; 4C086/MA60; 4C206/MA61; 4C084/MA63; 4C086/MA63; 4C206/MA63; 4C084/MA66; 4C086/MA66; 4C206/MA72; 4C206/MA80; 4C206/MA83; 4C206/MA86; 4C084/NA14; 4C086/NA14; 4C206/NA14; 4C084/ZB21.2; 4C084/ZB26.2; 4C086/ZB26; 4C206/ZB26; 4C084/ZC20.2; 4C086/ZC20; 4C206/ZC20; 4C084/ZC41.2; 4C086/ZC41; 4C206/ZC41

BASIC ABSTRACT:

WO 2001064217 A2 UPAB: 20050526

NOVELTY - Use of a combination of a nitrogen mustard or nitrosourea alkylating agent and a farnesyl protein transferase inhibitor for inhibiting growth of tumor cells is new.

DETAILED DESCRIPTION - Use of a combination of a nitrogen mustard or nitrosourea alkylating agent and one of 4 farnesyl transferase inhibitors e.g. a compound of formula (I), or their salts, is new.

Z = e.g. a group of formula (i);

T-U = -C(=X)N(R1)-, -C=N- or -C=N+(O-)-;

X = O or S;

R1 = H, 1-12C alkyl, Ar1, Ar2(1-6C alkyl), quinolinyl(1-6C alkyl), pyridyl(1-6C alkyl), hydroxy(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), mono or di(1-6C alkyl)amino(1-6C alkyl), amino(1-6C alkyl), -Alk1C(=O) R9, -Alk1-S(O)-R9 or -Alk1-S(O)2R9;

Alk1 = 1-6C alkanediyl;

R9 = OH, 1-6C alkyl, 1-6C alkyloxy, NH2, or 1-8C alkylamino optionally substituted with 1-6C alkyloxycarbonyl;

R2, R3, R16 = H, OH, halo, CN, 1-6C alkyl, 1-6C alkyloxy, hydroxy(1-6C alkyloxy), 1-6C alkyloxy(1-6C alkyloxy), amino(1-6C alkyloxy), mono- or di(1-6C alkyl)amino(1-6C alkyloxy), Ar1, Ar2(1-6C alkyl), Ar2oxy, Ar2(1-6C alkyloxy), hydroxycarbonyl, 1-6C alkyloxycarbonyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, or 4,4-dimethyloxazolyl; or

R2+R3 = -O-CH2-O-, -O-CH2-CH2-O-, -O-CH=CH-, -O-CH2 CH2-, -O-CH2-CH2-CH2- or -CH=CH-CH=CH- when on adjacent positions;

R4, R5 = H, halo, Ar1, 1-6C alkyl, hydroxy(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkyloxy, NH2, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl);

R6, R7 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxy, Ar2oxy, trihalomethyl, 1-6C alkylthio, or di(1-6C alkyl)amino; or

R6+R7 = -O-CH2-O- or -CH=CH-CH=CH- when on adjacent positions;

R8 = H, 1-6C alkyl, CN, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl(1-6C alkyl), cyano(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), carboxy(1-6C alkyl), hydroxy(1-6C alkyl), amino(1-6C alkyl), mono- or di(1-6C alkyl)amino(1-6C alkyl), imidazolyl, halo(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), aminocarbonyl(1-6C alkyl), -O-R10, -S-R10 or -N-R11-R12;

R10 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar1, Ar2(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), -Alk-OR13 or Alk- NR14R15;

R11 = H, 1-12C alkyl, Ar1 or Ar2(1-6C alkyl);

R12 = H, 1-6C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar1, Ar2(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), a natural amino acid, Ar1carbonyl, Ar2(1-6C alkyl)carbonyl, aminocarbonylcarbonyl, 1-6C alkyloxy(1-6C alkyl)carbonyl, OH, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino(1-6C alkyl)carbonyl, NH2, 1-6C alkylamino, 1-6C alkylcarbonylamino, -Alk2-OR13 or -Alk1 NR14R15;

R15 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar1 or Ar2(1-6C alkyl);

R14 = H, 1-6C alkyl, Ar1 or Ar2(1-6C alkyl);

R13 = R15 or hydroxy-(1-6C alkyl);

R17 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxycarbonyl or Ar1;

R18 = H, 1-6C alkyl, 1-6C alkyloxy or halo;

R19 = H or 1-6C alkyl; and

Ar1, Ar2 = phenyl optionally substituted with halo, 1-6C alkyl, 1-6C alkyloxy or CF3.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Farnesyl transferase inhibitor; Synergist.

Test methods are described but no results given.

USE - For inhibiting growth of tumor cells (claimed) and treating e.g. lung, pancreatic or colon cancer, myeloid leukemias, thyroid follicular cancer, myelodysplastic syndrome, tumors of mesenchymal origin, melanomas, teratocarcinomas, neuroblastomas, gliomas, benign tumor of the skin, or breast, kidney, ovary, bladder or epidermal carcinoma. Also for inhibiting benign and malignant proliferative diseases, where ras proteins are aberrantly activated as a result of oncogenic mutation in genes, e.g. neurofibromatosis.

ADVANTAGE - The combination provides a synergistic effect compared with use of the individual components. MANUAL CODE: CPI: B05-B01J; B06-D02; B06-D06; B06-D13; B06-D16;

B06-D17; B10-A03; B14-D06; B14-H01; B14-S09

TECH

PHARMACEUTICALS - Preferred Compounds: The nitrogen mustard or nitrosourea alkylating agent is preferably cyclophosphamide, chlorambucil, carmustine or lomustine.

ABEX DEFINITIONS - Full Definitions: The farnesyl transferase inhibitor is a compound of formula (I)-(IV). - Z = a group of formula (i) or (ii); - T-U = -C(=X)N(R1)-, -C=N- or -C=N+(O-)-; - X = O or S; - R1 = H, 1-12C alkyl, Ar1, Ar2(1-6C alkyl), quinolinyl(1-6C alkyl), pyridyl(1-6C alkyl), hydroxy(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), mono or di(1-6C alkyl)amino(1-6C alkyl), amino(1-6C alkyl), -Alk1C(=O) R9, -Alk1-S(O)-R9 or -Alk1-S(O)2R9; - Alk1 = 1-6C alkanediyl; - R9 = OH, 1-6C alkyl, 1-6C alkyloxy, NH2, or 1-8C alkylamino optionally substituted with 1-6C alkyloxycarbonyl; - R2, R3, R16 = H, OH, halo, CN, 1-6C alkyl, 1-6C alkyloxy, hydroxy(1-6C alkyloxy), 1-6C alkyloxy(1-6C alkyloxy), amino(1-6C alkyloxy), mono- or di(1-6C alkyl)amino(1-6C alkyloxy), Ar1, Ar2(1-6C alkyl), Ar2oxy, Ar2(1-6C alkyloxy), hydroxycarbonyl, 1-6C alkyloxycarbonyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, or 4,4-dimethyloxazolyl; or - R2+R3 = -O-CH2-O-, -O-CH2-CH2-O-, -O-CH=CH-, -O-CH2 CH2-, -O-CH2-CH2-CH2- or -CH=CH-CH=CH- when on adjacent positions; - R6, R7 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxy, Ar2oxy, trihalomethyl, 1-6C alkylthio, or di(1-6C alkyl)amino; or - R6+R7 = -O-CH2-O- or -CH=CH-CH=CH- when on adjacent positions; - R8 = H, 1-6C alkyl, CN, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl(1-6C alkyl), cyano(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), carboxy(1-6C alkyl), hydroxy(1-6C alkyl), amino(1-6C alkyl), mono- or di(1-6C alkyl)amino(1-6C alkyl), imidazolyl, halo(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), aminocarbonyl(1-6C alkyl), -O-R10, -S-R10 or -N-R11-R12; - R10 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar1, Ar2(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), -Alk-OR13 or Alk- NR14R15; - R11 = H, 1-12C alkyl, Ar1 or Ar2(1-6C alkyl); - R12 = H, 1-6C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar1, Ar2(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), a natural amino acid, Ar1carbonyl, Ar2(1-6C alkyl)carbonyl, aminocarbonylcarbonyl, 1-6C alkyloxy(1-6C alkyl)carbonyl, OH, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino(1-6C alkyl)carbonyl, NH2, 1-6C alkylamino, 1-6C alkylcarbonylamino, -Alk2-OR13 or -Alk1 NR14R15; - R15 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar1 or Ar2(1-6C alkyl); - R14 = H, 1-6C alkyl, Ar1 or Ar2(1-6C alkyl); - R13 = R15 or hydroxy-(1-6C alkyl); - R17 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxycarbonyl or Ar1; - R18 = H, 1-6C alkyl, 1-6C alkyloxy or halo; - R19 = H or 1-6C alkyl; - R4, R5 = H, Ar1, 1-6C alkyl, 1-6C alkyloxy(1-6C alkyl), 1-6C alkyloxy, 1-6C alkylthio, NH2, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl); - provided that: when Z = a group (ii), R1 and R2 are not

4,4-dimethyloxazolyl and R4 and R5 are not halo or 1-6C alkyloxy-1-6C alkyl; - R26, R27 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxy or Ar2oxy; - R28 = H, 1-6C alkyl, CN, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl(1-6C alkyl), cyano(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), hydroxycarbonyl(1-6C alkyl), hydroxy(1-6C alkyl), amino(1-6C alkyl), mono- or di(1-6C alkyl)amino(1-6C alkyl), halo(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), aminocarbonyl(1-6C alkyl), Ar1, Ar2(1-6C alkyloxy)(1-6C alkyl) or 1-6C alkylthio(1-6C alkyl); - -A- = -CH=CH-, -CH2-CH2-, -CH2-CH2-CH2-, -CH2-O-, -CH2-CH2-O-, -CH2-S-, CH2- CH2-S-, -CH=N-, -N=N- or -CO-NH-, where 1 H may be replaced by 1-4C alkyl or Ar1; - R31, R32 = H, OH, halo, CN, 1-6C alkyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, 1-6C alkyloxy, hydroxy(1-6C alkyloxy), 1-6C alkyloxy(1-6C alkyloxy), 1-6C alkyloxycarbonyl, amino(1-6C alkyloxy), mono- or di(1-6C alkyl)amino(1-6C alkyloxy), Ar2, Ar2(1-6C alkyl), Ar2-oxy or Ar2-(1-6C alkyloxy); or - R31+R32 = -O-CH2-O-, -O-CH2-CH2-O-, -O-CH=CH-, -O-CH2-CH2-, -O CH2-CH2-CH2- or -CH=CH-CH=CH- when on adjacent positions; - R33, R34 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxy, Ar3-oxy, 1-6C alkylthio, di(1-6C alkyl)amino, trihalomethyl or trihalomethoxy; or - R33+R34 = -CH2-O-, -O-CH2-CH2-O- or -CH=CH-CH=CH- when on adjacent positions; - R35 = 1-imidazolyl or 5-(1-R41)imidazolyl (both substituted by R43); - R43 = H, halo, Ar4, 1-6C alkyl, hydroxy(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkyloxy, 1-6C alkylthio, NH2, 1-6C alkyloxycarbonyl, 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl); - R44 = H, 1-6C alkyl or di(1-4C alkyl)aminosulfonyl; - R36 = H, OH, halo, 1-6C alkyl, CN, halo(1-6C alkyl), hydroxy(1-6C alkyl), cyano(1-6C alkyl), amino(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkylthio(1-6C alkyl), aminocarbonyl(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), 1-6C alkyloxycarbonyl, mono- or di(1-6C alkyl)amino(1-6C alkyl), Ar5, Ar5-(1-6C alkyloxy)(1-6C alkyl), -O-R37, -S-R37 or -NR38R39; - R37 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar6, Ar6-(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), -Alk-OR40 or -Alk-NR42; - R38 = H, 1-6C alkyl, Ar7 or Ar7-(1-6C alkyl); - R39 = H, 1-6C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar8, Ar8-(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), Ar8 carbonyl, Ar8-(1-6C alkylcarbonyl), aminocarbonyl-carbonyl, 1-6C alkyloxy(1-6C alkylcarbonyl), OH, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino(1-6C alkylcarbonyl), NH2, 1-6C alkylamino, 1-6C alkylcarbonylamino, -Alk-OR40 or -Alk-NR41R42; - Alk = 1-6C alkanediyl; - R40 = H, 1-6C alkyl, 1-6C alkylcarbonyl, hydroxy(1-6C alkyl), Ar9 or Ar9-(1-6C alkyl); - R41 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar10 or Ar10-(1-6C alkyl); - R42 = H, 1-6C alkyl, Ar11 or Ar11-(1-6C alkyl); - Ar1-Ar11 = phenyl optionally substituted with halo, 1-6C alkyl, 1-6C alkyloxy or CF3; - R51, R52 = H, OH, halo, CN, 1-6C alkyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, 1-6C alkyloxy, hydroxy(1-6C alkyloxy), 1-6C alkyloxy(1-6C alkyloxy), 1-6C alkyloxycarbonyl, amino(1-6C alkyloxy), mono- or di(1-6C alkyl)amino(1-6C alkyloxy), Ar1, Ar1(1-6C alkyl), Ar1-oxy or Ar1-(1-6C alkyloxy); - R53, R54 = H, halo, CN, 1-6C alkyl, 1-6C alkyloxy, Ar1-oxy, 1-6C alkylthio, di(1-6C alkyl)amino, trihalomethyl or trihalomethoxy; - R55 = H, halo, 1-6C alkyl, CN, halo(1-6C alkyl), hydroxy(1-6C alkyl), cyano(1-6C alkyl), amino(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkylthio(1-6C alkyl), aminocarbonyl(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), 1-6C alkyloxycarbonyl, mono- or di(1-6C alkyl)amino(1-6C alkyl), Ar1, Ar1(1-6C alkyloxy)(1-6C alkyl), -O-R10, -S-R10 or -N-R51R52; - R51 = H, 1-6C alkyl, Ar1 or Ar1(1-6C alkyl); - R52 = H, 1-6C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar1, Ar1(1-6C alkyl), 1-6C alkylcarbonyl-(1-6C alkyl), Ar1carbonyl, Ar1(1-6C alkylcarbonyl), aminocarbonylcarbonyl, 1-6C alkyloxy(1-6C alkylcarbonyl), OH, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino(1-6C alkylcarbonyl), NH2, 1-6C alkylamino, 1-6C alkylcarbonylamino, Alk-OR13 or Alk- NR14R15; -

R56 = 1-imidazolyl or 5-(1-R67)imidazolyl (both substituted by R66); - R66 = H, halo, Ar1, 1-6C alkyl, hydroxy(1-6C alkyl), 1-6C alkyloxy-(1-6C alkyl), 1-6C alkyloxy, 1-6C alkylthio, NH2, 1-6C alkyloxycarbonyl, 1-6C alkylthio(1-6C alkyl), 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl); - R67 = H, 1-6C alkyl or di(1-4C alkyl)aminosulfonyl; - R57 = H or 1-6C alkyl, provided that the dotted line does not represent a bond; - R58 = H, 1-6C alkyl, Ar2CH2 or Het1CH2; - R59 = H, 1-6C alkyl, 1-6C alkyloxy or halo; or - R58+R59 = -CH=CH-, -CH2-CH2-, -CH2-CH2-CH2, -CH2-O- or -CH2-CH2-O-; - Het1 = pyridinyl optionally substituted with 1 or 2 halo, 1-6C alkyl, 1-6C alkyloxy or CF3; - =X1-X2-X3- = =N-CR76=CR77-, =NN=CR76-, =N-NH-C(=O)-, =N-N=N, =N-CR76=N-, =CR76-CR77=CR78-, =CR76-N=CR77-, =CR76-NH-C(=O)- or =CR76-N=N-; - R76-R78 = = H, 1-4C alkyl, OH, 1-4C alkyloxy, aryloxy, 1-4C alkyloxycarbonyl, hydroxy(1-4C alkyl), 1-4C alkyloxy(1-4C alkyl), mono- or di(1-4C alkyl)amino(1-4C alkyl), CN, NH2, thio, 1-4C alkylthio, arylthio or aryl; - Y1, Y2 = CH CHR79-, C=N-, CH-NR79- or C=CR79; - R79 = H, halo, halocarbonyl, aminocarbonyl, hydroxy(1-4C alkyl), CN, carboxyl, 1-4C alkyl, 1-4C alkyloxy, 1-4C alkyloxy(1-4C alkyl), 1-4C alkyloxycarbonyl, mono- or di(1-4C alkyl)amino, mono- or di(1-4C alkyl)amino(1-4C alkyl), or aryl; - r = 0-5; - s = 0-5; - t = 0-3; - R71, R72 = OH, halo, CN, 1-6C alkyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, 1-6C alkyloxy, hydroxy(1-6C alkyloxy), 1-6C alkylthio, 1-6C alkyloxy(1-6C alkyloxy), 1-6C alkyloxycarbonyl, amino(1-6C alkyloxy), mono- or di(1-6C alkyl)amino, mono- or di(1-6C alkyl)amino(1-6C alkyloxy), aryl, aryl(1-6C alkyl), aryloxy, aryl(1-6C alkyloxy), hydroxycarbonyl, 1-6C alkyloxycarbonyl, aminocarbonyl, amino(1-6C alkyl), mono- or di(1-6C alkyl)aminocarbonyl, mono- or di(1-6C alkyl)amino(1-6C alkyl); or - R71+R72 = -O-CH2-O-, -O-CH2-CH2-O-, -O CH=CH-, -O-CH2-CH2-, -O-CH2-CH2-CH2- or -CH=CH-CH=CH- provided they are adjacent to each other; - R73 = H, halo, 1-6C alkyl, CN, halo(1-6C alkyl), hydroxy(1-6C alkyl), cyano(1-6C alkyl), amino(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkylthio(1-6C alkyl), aminocarbonyl(1-6C alkyl), hydroxycarbonyl, hydroxycarbonyl(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), 1-6C alkylcarbonyl(1-6C alkyl), 1-6C alkyloxycarbonyl, aryl, aryl(1-6C alkyloxy)(1-6C alkyl), mono or di(1-6C alkyl)amino(1-6C alkyl), -O-R80, -S-R80 or NR81R82; - R80 = H, 1-6C alkyl, 1-6C alkylcarbonyl, aryl, aryl(1-6C alkyl), 1-6C alkyloxycarbonyl(1-6C alkyl), -Alk-OR83 or -Alk-NR84R85; - R81 = H, 1-6C alkyl, aryl or aryl(1-6C alkyl); - R82 = H, 1-6C alkyl, aryl, OH, NH2, 1-6C alkyloxy, 1-6C alkylcarbonyl(1-6C alkyl), aryl(1-6C alkyl), 1-6C alkylcarbonylamino, mono- or di(1-6C alkyl)amino, 1-6C alkylcarbonyl, aminocarbonyl, arylcarbonyl, halo(1-6C alkylcarbonyl), aryl(1-6C alkylcarbonyl), 1-6C alkyloxycarbonyl, 1-6C alkyloxy(1-6C alkylcarbonyl), mono- or di(1-6C alkyl)aminocarbonyl (where alkyl is optionally substituted by 1 or more aryl or 1-3C alkyloxycarbonyl), aminocarbonylcarbonyl, mono- or di(1-6C alkyl)amino(1-6C alkylcarbonyl), -Alk-OR83 or -Alk-NR84R85; - R85 = H, 1-6C alkyl, 1-6C alkylcarbonyl, aryl or aryl(1-6C alkyl); - R84 = H, 1-6C alkyl, aryl or aryl(1-6C alkyl); - R83 = R85 or hydroxy-(1-6C alkyl); - R74 = 1-imidazolyl or 5-(1-R87)imidazolyl (both substituted by R86); - R86 = H, halo, aryl, 1-6C alkyl, hydroxy(1-6C alkyl), 1-6C alkyloxy-(1-6C alkyl), 1-6C alkyloxy, 1-6C alkylthio, NH2, mono- or di(1-4C alkyl)amino, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylthio(1-6C alkyl), 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl); - provided that if R86 is bound to an N in the imidazole ring, it may be only H, aryl, 1-6C alkyl, hydroxy(1-6C alkyl), 1-6C alkyloxy(1-6C alkyl), 1-6C alkyloxycarbonyl, 1-6C alkylS(O)(1-6C alkyl) or 1-6C alkylS(O)2(1-6C alkyl); - R87 = H, 1-6C alkyl, 1-6C alkyloxy(1-6C alkyl), aryl(1-6C alkyl), CF3 or di(1-4C alkyl)aminosulfonyl; - R75 = 1-6C alkyl, 1-6C alkyloxy or halo; and - aryl = naphthalenyl, or phenyl optionally substituted with 1 or more halo, 1-6C alkyl, 1-6C alkyloxy or CF3.

ADMINISTRATION - Administration of the nitrogen mustard or nitrosourea

alkylating agent and farnesyl transferase inhibitor is 100-500 mg/m2 and 0.0001-100 preferably 0.001-10 mg/kg respectively, preferably orally, rectally, percutaneously or by parenteral injection. Typically, the farnesyl transferase inhibitor is administered at 100 or 200 mg twice daily for 7, 14, 21 or 28 days, and nitrogen mustard or nitrosourea alkylating agent is administered once or twice per course of treatment, which may be repeated every 7, 14, 21 or 28 days.

SPECIFIC COMPOUNDS - Combinations including 7 farnesyl transferase inhibitors are claimed, e.g. 4-(3-chlorophenyl)-6-((4 chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)-methyl)-1-methyl 2(1H)-quinolinone.

EXAMPLE - No suitable example given.

AN.S DCR-450722

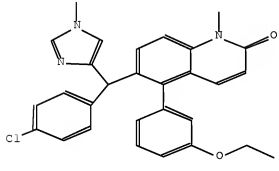
CN.S 6-[(4-Chloro-phenyl)-(1-methyl-1H-imidazol-4-yl)-methyl]-5-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one hydrochloride

SDCN RA56U2

CM 1

Cl

CM 2



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ACCESSION NUMBER: 2001-536460 [59] WPIX

DOC. NO. CPI: C2001-159700 [59]

TITLE: Pharmaceutical composition useful in the treatment of advanced breast cancer comprises a farnesyl protein transferase inhibitor

DERWENT CLASS: B02

INVENTOR: HORAK D; HORAK I; HORAK I D; PALMER J P; PALMER P A; PALMER P A J P

PATENT ASSIGNEE: (HORA-I) HORAK I D; (JANC-C) JANSSEN PHARM NV; (PALM-I) PALMER P A

COUNTRY COUNT: 93

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC

WO	2001056552	A2	20010809 (200159)*	EN	41[0]
AU	2001033726	A	20010814 (200173)	EN	
EP	1255537	A2	20021113 (200282)	EN	
US	20030027839	A1	20030206 (200313)	EN	
JP	2003521509	W	20030715 (200347)	JA	68
US	20040192726	A1	20040930 (200465)	EN	
EP	1255537	B1	20060419 (200630)	EN	
DE	60118889	E	20060524 (200635)	DE	
ES	2262626	T3	20061201 (200680)	ES	
DE	60118889	T2	20061130 (200716)	DE	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001056552	A2	WO 2001-EP1032	20010201
AU 2001033726	A	AU 2001-33726	20010201
DE 60118889	E	DE 2001-618889	20010201
EP 1255537	A2	EP 2001-905717	20010201
EP 1255537	B1	EP 2001-905717	20010201
DE 60118889	E	EP 2001-905717	20010201
ES 2262626	T3	EP 2001-905717	20010201
JP 2003521509	W	JP 2001-556244	20010201
EP 1255537	A2	WO 2001-EP1032	20010201
US 20030027839	A1	WO 2001-EP1032	20010201
JP 2003521509	W	WO 2001-EP1032	20010201
US 20040192726	A1 Cont of	WO 2001-EP1032	20010201
EP 1255537	B1	WO 2001-EP1032	20010201
DE 60118889	E	WO 2001-EP1032	20010201
US 20030027839	A1	US 2002-203083	20020802
US 20040192726	A1 Cont of	US 2002-203083	20020802
US 20040192726	A1	US 2004-818767	20040406
DE 60118889	T2	DE 2001-618889	20010201
DE 60118889	T2	EP 2001-905717	20010201
DE 60118889	T2	WO 2001-EP1032	20010201

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
DE 60118889	E	Based on	EP 1255537	A
ES 2262626	T3	Based on	EP 1255537	A
AU 2001033726	A	Based on	WO 2001056552	A
EP 1255537	A2	Based on	WO 2001056552	A
JP 2003521509	W	Based on	WO 2001056552	A
EP 1255537	B1	Based on	WO 2001056552	A
DE 60118889	E	Based on	WO 2001056552	A
DE 60118889	T2	Based on	EP 1255537	A
DE 60118889	T2	Based on	WO 2001056552	A

PRIORITY APPLN. INFO: EP 2000-200373 20000204
INT. PATENT CLASSIF.:

MAIN:	A61K031-00; A61K045-00
SECONDARY:	A61K031-138; A61K031-4709; A61K031-4745; A61K031-517; A61K031-519; A61P035-00; A61P035-04; A61P043-00; C07D401-06
IPC ORIGINAL:	A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-00 [I,A]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61K0031-4709 [I,A]; A61K0031-4738 [I,C]; A61K0031-4738 [I,C];

A61K0031-4745 [I,A]; A61K0031-4745 [I,A]; A61K0031-517 [I,A]; A61K0031-517 [I,C]; A61K0031-517 [I,A]; A61K0031-519 [I,A]; A61K0031-519 [I,C]; A61K0031-519 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,A]; A61P0035-04 [I,A]; A61P0035-04 [I,A]; A61K0031-00 [I,C]; A61K0031-4709 [I,C]; A61K0031-4738 [I,C]; A61K0031-517 [I,C]; A61K0031-519 [I,C]; A61P0035-00 [I,C]

IPC RECLASSIF.: A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-138 [I,A]; A61K0031-138 [I,C]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61K0031-4738 [I,C]; A61K0031-4745 [I,A]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61K0045-06 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-04 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; C07D0401-00 [I,C]; C07D0401-06 [I,A]

ECLA: A61K0031-00; A61K0031-138+M; A61K0031-4709; A61K0031-4745; A61K0045-06

USCLASS NCLM: 514/312.000

NCLS: 514/314.000

JAP. PATENT CLASSIF.:

MAIN/SEC.: A61K0031-138; A61K0031-4709; A61K0045-00; A61P0035-00; A61P0043-00 111; C07D0401-06

FTERM CLASSIF.: 4C063; 4C084; 4C086; 4C201; 4C206; 4C063/AA01; 4C086/AA01; 4C206/AA01; 4C086/AA02; 4C206/AA02; 4C084/AA17; 4C063/BB03; 4C086/BC38; 4C063/CC25; 4C063/DD14; 4C063/EE01; 4C206/FA23; 4C086/GA07; 4C084/MA01; 4C086/MA01; 4C086/MA02; 4C206/MA02; 4C086/MA04; 4C206/MA04; 4C084/NA14; 4C086/NA14; 4C206/NA14; 4C084/ZB26.2; 4C086/ZB26; 4C206/ZB26; 4C084/ZC20.2; 4C086/ZC20; 4C086/ZC75; 4C206/ZC75

BASIC ABSTRACT:

WO 2001056552 A2 UPAB: 20060117

NOVELTY - Pharmaceutical composition comprises a farnesyl protein transferase inhibitor.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Farnesyl protein transferase inhibitor.

USE - In the treatment of advanced breast cancer (claimed)

ADVANTAGE - The inhibitor shows shrinkage of the tumor rather than simple delaying the tumor progression. MANUAL CODE: CPI: B06-H; B10-B04B; B14-D06; B14-H01

TECH

ORGANIC CHEMISTRY - Preferred Compounds: The inhibitor is of formula (I), (II), (III), (IV), (V), (VI), (VII), (VIII) or (IX), their stereoisomeric form, acid or base addition salt:

X = oxygen or sulfur (preferably oxygen);

R1 = H, 1-12C alkyl, Ar1, Ar2 1-6C alkyl, quinolinyl 1-6C alkyl, pyridyl 1-6C alkyl, hydroxy 1-6C alkyl, 1-6C alkoxy 1-6C alkyl, mono- or di-(1-6C alkyl)amino 1-6C alkyl, amino 1-6C alkyl, -Alk1-C(=O)-R9, -Alk1-S(O)-R9 or Alk1-S(O)2-R9 (preferably H, 1-6C alkyl, 1-6C alkyloxyl-6C alkyl, mono- or di(1-6C alkyl)amino1-6C alkyl);

Alk1 and Alk2 = 1-6C alkanediyl;

R9 = hydroxy, 1-6C alkyl, 1-6C alkyloxy, amino or 1-8C alkylamino (optionally substituted by 1-6C alkyloxycarbonyl);

R2, R3 and R16 = H, hydroxy, halo, cyano, 1-6C alkyl, 1-6C alkyloxy, hydroxy 1-6C alkyloxy, 1-6C alkyloxy 1-6C alkyloxy, amino 1-6C alkyloxy, mono- or di(1-6C alkyl)amino 1-6C alkyloxy, Ar1, Ar2 1-6C alkyl, Ar2oxy, Ar2 1-6C alkyloxy, hydroxycarbonyl, 1-6C alkyloxycarbonyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl or 4,4-dimethyloxazolyl (preferably R3 is H and R2 is halo, 1-6C alkyl, 2-6C alkenyl, 1-6C alkyloxy, trihalomethoxy or hydroxy 1-6C alkyloxy); or

R2+R3 and R'2+R'3 = -O-CH2-O-, -O-CH2-CH2-O-, -O-CH=CH-, -O-CH2-CH2-,

-O-CH2-CH2-CH2- or -CH=CH-CH=CH-;
R4 and R5 = hydrogen, halo, Ar1, 1-6C alkyl, hydroxy-1-6C alkyl, 1-6C alkyloxy1-6C alkyl, 1-6C alkoxy, 1-6C alkylthio, amino, hydroxycarbonyl, 1-6C alkoxycarbonyl, 1-6C alkylS(O)1-6C alkyl or 1-6C alkylS(O)2-1-6C alkyl;
R6 and R7 = hydrogen, halo, cyano, 1-6C alkyl, 1-6C alkyloxy, Ar2oxy, trihalomethyl, 1-6C alkylthio or di(1-6C alkyl)amino; or
R6+R7 = -O-CH2-O- or -CH=CH-CH=CH-;
R8 = H, 1-6C alkyl, cyano, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl 1-6C alkyl, cyano 1-6C alkyl, 1-6C alkyloxycarbonyl 1-6C alkyl, carboxy 1-6C alkyl, hydroxy 1-6C alkyl, amino 1-6C alkyl, mono- or di-(1-6C alkyl) amino 1-6C alkyl, imidazolyl, halo 1-6C alkyl, 1-6C alkyloxy 1-6C alkyl, aminocarbonyl 1-6C alkyl, -OR10, -SR10 or -N-R11R12 (preferably H, hydroxy, halo1-6C alkyl, hydroxy 1-6C alkyl, cyano1-6C alkyl, 1-6C alkyloxycarbonyl1-6C alkyl, imidazolyl or -NR11R12);
R10 = H, 1-6C alkyl, 1-6C alkyl carbonyl, Ar1, Ar2 1-6C alkyl, 1-6C alkyloxycarbonyl 1-6C alkyl, Alk2-OR13 or Alk2-NR14R15;
R11 = H, 1-12C alkyl, Ar1 or Ar2 1-6C alkyl (preferably H or 1-12C alkyl);
R12 = H, 1-6C alkyl, 1-16C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar1, Ar2-1-6C alkyl, 1-6C alkylcarbonyl 1-6C alkyl, natural amino acid, Ar1 carbonyl, Ar2 1-6C alkylcarbonyl, aminocarbonyl carbonyl, 1-6C alkyloxy 1-6C alkyl carbonyl, hydroxy, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino1-6Calkylcarbonyl, amino, 1-6C alkylamino, 1-6C alkylcarbonylamino, Alk2-OR13 or Alk2-NR14R15 (preferably H, 1-6C alkyl, 1-6C alkyloxy, 1-6C alkyloxyl-6C alkylcarbonyl, hydroxy, -Alk2-OR13);
R14 = H, 1-6C alkyl, Ar1 or Ar2 1-6C alkyl;
R13 = R14, 1-6C alkylcarbonyl or hydroxy 1-6C alkyl (preferably H or 1-6C alkyl);
R15 = R14 or 1-6C alkylcarbonyl;
R17 = H, halo cyano, 1-6C alkyl, 1-6C alkyloxycarbonyl or Ar1;
R18 = H, 1-6C alkyl, 1-6C alkyloxy or halo;
R19 = H or 1-6C alkyl;
Ar1 and Ar2 = phenyl (optionally substituted by 1-6C alkyl, hydroxy, amino, 1-6C alkyloxy or halo);
R'2 and R'3 = R2 (except 4,4-dimethyloxazolyl);
R'4 and R'5 = R4 (except halo and hydroxy 1-6C alkyl);
R'6 and R'7 = H, halo, cyano, 1-6C alkyl, 1-6C alkyloxy or Ar2oxy;
R'8 = hydrogen, 1-6C alkyl, cyano, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl 1-6C alkyl, cyano 1-6C alkyl, 1-6C alkyloxycarbonyl 1-6C alkyl, hydroxycarbonyl 1-6C alkyl, hydroxy 1-6C alkyl, amino 1-6C alkyl, mono- or di(1-6C alkyl)amino1-6Calkyl, halo1-6Calkyl, 1-6Calkyloxy1-6Calkyl, aminocarbonyl1-6C alkyl, Ar1, Ar21-6Calkyloxy1-6Calkyl or 1-6C alkylthio1-6C alkyl;
A = -CH=CH-, -CH2-CH2-, -CH2-CH2-CH2-, -CH2-O-, -CH2-CH2-O-, -CH2-S-, -CH2-CH-2-S-, -CH=N-, -N=N- or -CO-NH- (all optionally substituted by 1-4C alkyl or Ar'1);
R1, R2, R'1 and R'2 = H, hydroxy, halo, cyano, 1-6C alkyl, trihalomethoxy, 2-6C alkenyl, 1-6C alkyloxy, hydroxyl-6Calkyloxy, 1-6C alkyloxyl-6Calkyloxy, 1-6C alkyloxycarbonyl, amino1-6Calkyloxy, mono- or di(1-6C alkyl)amino 1-6C alkyloxy, Ar'2, Ar'2 1-6Calkyl, Ar'2-oxy or Ar'21-6C alkyloxy; or
R1+R2 and R'1+R'2 = -O-CH2-O-, -O-CH2-CH2-O-, -O-CH=CH-, -O-CH2-CH2-, -O-CH2-CH2-CH-2- or -CH=CH-CH=CH-;
R3, R4, R'3 and R'4 = H, halo, cyano, 1-6C alkyl, 1-6C alkyloxy, Ar'3-oxy, 1-6C alkylthio, di(1-6C alkyl)thio, trihalomethyl or trihalomethoxy; or
R3+R4 = -O-CH2-O-, -o-CH2-CH2-O- or -CH=CH-CH=CH-;
R5 = imidazole-1-yl (substitued by R'13) or imidazole-5-yl (substituted on 1-position by R'14 and other positions by R'13);
R'13 = H, halo, Ar'4, 1-6C alkyl, hydroxyl-6C alkyl, 1-6C alkyloxy-1-6C

alkyl, 1-6C alkyloxy, 1-6C alkylthio, amino, 1-6C alkyloxycarbonyl, 1-6C alkylS(O)1-6C alkyl or 1-6C alkylS(O)21-6C alkyl;
R'14 = H, 1-6C alkyl or di(1-4C alkyl)aminosulfonyl;
R6 = H, hydroxy, halo, 1-6C alkyl, cyano, halo1-6C alkyl, hydroxy1-6C alkyl, cyano1-6C alkyl, amino 1-6C alkyl, 1-6C alkyloxy1-6C alkyl, 1-6C alkylthio1-6C alkyl, aminocarbonyl1-6C alkyl, 1-6C alkyloxycarbonyl1-6C alkyl, 1-6C alkylcarbonyl1-6C alkyl, 1-6C alkyloxycarbonyl, mono- or di(1-6C alkyl) amino1-6C alkyl, Ar'5, Ar'5-1-6Calkyloxy-1-6C alkyl, -O-R7, -S-R7 or -N-R8R9;
R7 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar'6, Ar'6-1-6C alkyl, 1-6C alkyloxycarbonyl1-6C alkyl, -Alk1-OR10 or -Alk1-NR11R12;
R8 = H, 1-6C alkyl, Ar'7 or Ar'7-1-6C alkyl;
R9 = H, 1-6C alkyl, 1-16C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylaminocarbonyl, Ar'8, Ar'8-1-6C alkyl, 1-6C alkylcarbonyl 1-6C alkyl, Ar'8 carbonyl, Ar'8-1-6C alkylcarbonyl, aminocarbonyl carbonyl, 1-6C alkyloxy 1-6C alkyl carbonyl, hydroxy, 1-6C alkyloxy, aminocarbonyl, di(1-6C alkyl)amino1-6Calkylcarbonyl, amino, 1-6C alkylamino, 1-6C alkylcarbonylamino, Alk2-OR10 or Alk2-NR11R12;
R10 = H, 1-6C alkyl, 1-6C alkylcarbonyl, hydroxy-1-6C alkyl, Ar'9 or Ar'9-1-6C alkyl;
R11 = H, 1-6C alkyl, 1-6C alkylcarbonyl, Ar'10 or Ar'10-1-6C alkyl;
R12 = H, 1-6C alkyl, Ar'11 or Ar'11-1-6C alkyl;
Ar'1 - Ar'11 = phenyl (optionally substituted by halo, 1-6C alkyl, 1-6C alkyloxy or trifluoromethyl;
R'5 = R6 (except hydroxy);
R'6 = imidazole-1-yl (substituted by R16) or imidazole-5-yl (substitued on 1-position by R17 and other positions by R16);
R16 = H, halo, Ar'1, 1-6C alkyl, hydroxy1-6C alkyl, 1-6C alkyloxy-1-6C alkyl, 1-6C alkyloxy, 1-6C alkylthio, amino, 1-6C alkyloxycarbonyl, 1-6C alkylthio1-6C alkyl, 1-6C alkylS(O)1-6C alkyl or 1-6C alkylS(O)21-6C alkyl;
R17 = H, 1-6C alkyl or di(1-4C alkyl)aminosulfonyl;
R'7 = H or 1-6C alkyl (if the dotted line does not represent a bond);
R'8 = H, 1-6C alkyl, Ar'2CH2 or Het1CH2;
R'9 = H, 1-6C alkyl, 1-6C alkyloxy or halo;
R'8+R'9 = -CH=CH-, -CH2-CH2-, -CH2-CH2-CH2-, -CH2-O- or -CH2-CH2-O-;
Het1 = pyridinyl (optionally mono- or di-substituted with halo, 1-6C alkyl, 1-6C alkyloxy or trifluoromethyl);
X1-X2-X3 = =N-CR6=CR7-, =CR6-CR7=CR8-, =N-N=CR6-, =CR6-N=CR7-, =N-NH-C(=O)-, =CR6-NH-C(=O)-, =N-N=N-, =CR6-N=N- or =N-CR6=N- (preferably =N-N=CR6- =N-NH-C(=O)- or =N-N=N-);
R6, R7 and R8 = H, 1-4C alkyl, hydroxy, 1-4C alkyloxy, aryloxy, 1-4C alkyloxycarbonyl, hydroxy(1-4C)alkyl, 1-4C alkyloxy(1-4C)alkyl, mono- or di(1-4C alkyl)amino1-4C alkyl, cyano, amino, thio, 1-4C alkylthio, arylthio or aryl (preferably R6 is 1-4C alkyl);
-Y1-Y2- = =CH-CHR9-, =C=N-, =CH-NR9- or =C=CR9- (preferably =C=N-, =CH-NR9- or =C=CR9-);
R9 = H, halo, halocarbonyl, aminocarbonyl, hydroxy 1-4C alkyl, cyano, carboxyl, 1-4c alkyl, 1-4C alkyloxy, 1-4C alkyloxyl-4C alkyl, 1-4C alkyloxycarbonyl, mono- or di(1-4C alkyl)amino, mono- or di(1-4C alkyl)amino1-4Calkyl or aryl (preferably H);
r and s = 0 - 5 (preferably 1);
t = 0 - 3 (preferably 0);
R1 and R2 = hydroxy, halo, cyano, 1-6C alkyl, trihalomethyl, trihalomethoxy, 2-6C alkenyl, 1-6C alkyloxy, hydroxy 1-6C alkyloxy, 1-6C alkylthio, 1-6C alkyloxyl-6Calkyloxy, 1-6C alkyloxycarbonyl, amino1-6C alkyloxy, mono- or di(1-6C alkyl)amino, mono- or di(1-6C alkyl)amino1-6Calkyloxy, aryl, aryl1-6Calkyl, aryloxy, aryl1-6Calkyloxy, hydroxycarbonyl, 1-6C alkyloxycarbonyl, aminocarbonyl, amino1-6Calkyl, mono- or di(1-6C alkyl)aminocarbonyl, mono- or di(1-6C alkyl)amino1-6C

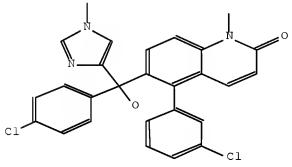
alkyl (preferably R1 is halo or 1-4C alkyl, especially 3-chloro or 3-methyl, and R2 is halo, especially 4-chloro);
R3 = H, halo, 1-6C alkyl, cyano, halo(1-6C) alkyl, hydroxy(1-6C)alkyl, cyano(1-6C)alkyl, amino(1-6C)alkyl, 1-6C alkyloxy 1-6C alkyl, 1-6C alkylthio 1-6C alkyl, aminocarbonyl 1-6C alkyl, hydroxycarbonyl, hydroxycarbonyl (1-6C) alkyl, 1-6C alkyloxycarbonyl 1-6C alkyl, 1-6C alkylcarbonyl 1-6C alkyl, 1-6C alkyloxycarbonyl, aryl, aryl1-6Calkyloxyl-6C alkyl, mono- or di(1-6C alkyl)amino1-6C alkyl, -O-R10, -S-R10 or -NR11R12 (preferably -O-R10 or -NR11R12);
R10 = H, 1-6C alkyl, 1-6C alkylcarbonyl, aryl, aryl-1-6C-alkyl, 1-6C alkyloxycarbonyl-1-6C alkyl, -Alk1-OR13 or Alk1-NR14R15 (preferably H);
R11 = H, 1-6C alkyl, aryl or aryl(1-6C)alkyl (preferably H);
R12 = H, 1-6C alkyl, aryl, hydroxy, amino, 1-6C alkyloxy, 1-6C alkylcarbonyl1-6C alkyl, aryl 1-6C alkyl, 1-6C alkylcarbonylamino, mono- or di(1-6C alkyl) amino, 1-6C alkylcarbonyl, aminocarbonyl, arylcarbonyl, halo 1-6C alkylcarbonyl, aryl 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkyloxyl-6Calkylcarbonyl, mono- or di(1-6C alkyl)aminocarbonyl (where the alkyl is optionally substituted by at least one aryl, 1-3C alkyloxycarbonyl, aminocarbonylcarbonyl, mono- or di(1-6C alkyl)amino1-6C alkylcarbonyl, -Alk1-OR13 or -Alk1-NR14R15) (preferably H or hydroxy);
R13 = H, 1-6C alkyl, 1-6C alkylcarbonyl, hydroxyl-6C alkyl, aryl or aryl1-6C alkyl;
R14 = H, 1-6C alkyl, aryl or aryl1-6C alkyl;
R15 = H, 1-6C alkyl, 1-6C alkylcarbonyl, aryl or aryl 1-6C alkyl;
R4 = imidazole-1-yl (substitued by R16) or imidazole-5-yl (substitued on 1-position by R17 and other positions by R16) (preferably imidazole-5-yl (substitued on 1-position by R17 and other positions by R16));
R16 = H, halo, aryl, 1-6C alkyl, hydroxyl-6C alkyl, 1-6C alkyloxy-1-6C alkyl, 1-6C alkyloxy, 1-6C alkylthio, amino, mono- or di(1-4C alkyl)amino, hydroxycarbonyl, 1-6C alkyloxycarbonyl, 1-6C alkylthiol-6C alkyl, 1-6C alkyl-S(O)1-6C alkyl, 1-6C alkyl-S(O)21-6C alkyl or may be bound to one nitrogen atom in the imidazole ring (when bound to the nitrogen R16 is H, aryl, 1-6C alkyl, hydroxyl-6C alkyl, 1-6C alkyloxyl-6C alkyl, 1-6C alkyloxycarbonyl, 1-6C alkyl-S(O)1-6C alkyl or 1-6C alkyl-S(O)21-6C alkyl;
R17 = H, 1-6C alkyl, 1-6C alkyloxyl-6C alkyl, aryl1-6C alkyl, trifluoromethyl or di(1-4C alkyl)aminosulfonyl;
R5 = 1-6C alkyl, 1-6C alkyloxy or halo.
The aryl is phenyl (optionally substituted by at least one halo, 1-6C alkyl, 1-6C alkyloxy or trifluoromethyl) or naphthalenyl. The inhibitor is administered in combination with an additional anti-cancer agent (preferably tamoxifen).

ABEX ADMINISTRATION - The compounds are administered orally, parenterally or transdermally. Dosage is from 10 - 1500 mg/Day (preferably 100 - 1000 mg/Day).

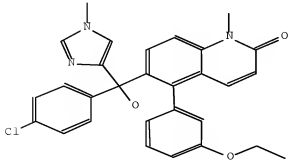
SPECIFIC COMPOUNDS - 4-(3-Chlorophenyl)-6-((4-chlorophenyl)hydroxy(1-methyl-1H imidazol-5-yl)methyl)-1-methyl-2(1H)-quinolinone, 6-(amino(4-chlorophenyl)-1-methyl-1H-imidazol-5-ylmethyl)-4-(3-chlorophenyl)1-methyl-2(1H)-quinolinone, 6-((4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-ethoxyphenyl)-1 methyl-2(1H)-quinolinone, 6-((4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone monohydrochloride.monohydrate, 6-(amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone, 6-amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-1-methyl-4-(3-propylphenyl)-2(1H)-quinolinone, (+)-6-(amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone or 5-(3-chlorophenyl)-alpha-(4-chlorophenyl)-alpha-(1-methyl-1H-imidazol-5-yl)tetrazolo(1,5-a)quinazoline-7-methanamine are specifically claimed as the farnesyl protein transferase inhibitor.

EXAMPLE - (+)-6-(Amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone (A) was tested in 27 patients with advanced breast cancer. The median age of the patients was 59 years (range 35 - 80 years). The first 6 patients treated with (A) (4 mg) developed grade 3/4 neutropenia after a median of 26 days, 5 were re-treated with dose reduction following neutrophil recovery without further haematological toxicity. The subsequent 21 patients received (A) (300 mg) in which 6 (29%) developed grade 3/4 neutropenia after a median of 32 days, with one episode of fever. Neutrophil recovery occurred over 1 - 2 weeks in all cases. Thrombocytopenia (grade 3) occurred in 3 (11%) patients. 26 patients were able to be evaluated for tumour response, 8 withdrew early (less than 12 weeks) due to either progression of disease and/or toxicity while 18 patients received at least 3 months treatment (range 12 - more than 36 weeks). Tumor shrinkage of at least 50% in volume was seen in 3 (12%) patients, sites of response included liver, lung, lymph nodes and skin nodules. A further 9 (35%) patients had stable disease, showing no progression of tumor growth, at 3 month evaluation.

AN.S DCR-450670
CN.S 5-(3-Chloro-phenyl)-6-[(4-chloro-phenyl)-hydroxy-(1-methyl-1H-imidazol-4-yl)-methyl]-1-methyl-1H-quinolin-2-one
SDCN RA56SN



AN.S DCR-450672
SDCN RA56SP

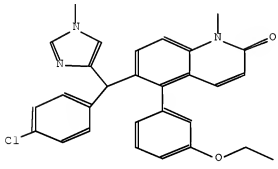


AN.S DCR-450722
CN.S 6-[(4-Chloro-phenyl)-(1-methyl-1H-imidazol-4-yl)-methyl]-5-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one hydrochloride
SDCN RA56U2

CM 1

Cl

CM 2



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ACCESSION NUMBER: 2008-12867 BIOTECHDS Full-text
TITLE: New quinolinone derivatives useful for treating e.g. vascular stroke, cardiovascular disorders, inflammation, gout, arthritis, atherosclerosis, diabetes, osteoarthritis, cachexia and cancer;
pharmaceutical composition comprising quinolinone derivative, useful in treatment of stroke, cardiovascular disease, inflammatory disease, arteriosclerosis, diabetes, osteoarthritis and cancer
AUTHOR: VIALARD J E; ANGIBAUD P R; MEVELLEC L A; MEYER C; FREYNE E J E; PILATTE I N C; ROUX B; PASQUIER E T J; BOURDREZ X M; ADELINET C D; MARCONNET-DECRANE L F; MACRITCHIE J A; DUFFY J E S; OWENS A P; STORCK P; PONCELET V S
PATENT ASSIGNEE: JANSSEN PHARM NV
PATENT INFO: WO 2008107478 12 Sep 2008
APPLICATION INFO: WO 2008-EP52764 7 Mar 2008

PRIORITY INFO: US 2007-893680 8 Mar 2007; EP 2007-103788 8 Mar 2007
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2008-N22686 [77]
AB DERWENT ABSTRACT:
NOVELTY - Quinolinone derivatives, their N-oxide forms, addition salts or stereo-chemically isomeric forms are new.
DETAILED DESCRIPTION - Quinolinone derivatives of formula (I), their N-oxide forms, addition salts or stereo-chemically isomeric forms are new. m=0-2; n=0-4; X=direct bond, CR10R11, (C=O)NR8, NR8, O or C?=C; R1=aryl or Het (where two carbon atoms on aryl or Het optionally bridged (i.e. forming bi- or tricyclic group) with a bivalent radical selected from -O-CH2-CH2-O-, -CH2-O-CH2-O-, -O-CH2-CH2-CH2-, -O-CH2-CH2-NR8-, -O-C(R8)2-O-, -O-CH2-CH2-, -CH2-N-CH2-CH2-, -(CH2)3- or -(CH2)4-; and optionally bridged aryl or Het each optionally mono- to penta-substituted by H, halo, cyano, nitro, hydroxycarbonyl, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, amino-3-6C cycloalkyl, halo-1-6C alkyl, trihalo-1-6C alkyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, 2-6C alkenylcarbonyl, oxime, 1-6C alkyloxime, amidoxime, -C=C-CH2O-CH3, -C?=C-CH2N(CH3)2, -C?=C-Si(CH3)3, hydroxy-1-6C alkyl, hydroxy-2-6C alkenyl, hydroxy-2-6C alkynyl, cyano-1-6C alkyl, cyano-2-6C alkenyl, aminocarbonyl-1-6C alkyl, 1-6C alkylsulfonyl-1-6C alkyl, 1-6C alkylsulfonyl-2-6C alkenyl, 1-6C alkylsulfonyl-1-6C alkynyl, -PO(O-1-6C alkyl)2, -B(OH)2, -S-CH3, SF5, 1-6C alkylsulfonyl, -NR8R9, 1-6C alkyl-NR8R9, -OR8, -1-6C alkyl-OR8, -CONR8R9, piperidinyl-1-6C alkyl, piperazinyl-1-6C alkyl, 1-6C alkylpiperazinyl-1-6C alkyl, morpholinyl-1-6C alkyl, T2, 1-6C alkylpiperazinyl, morpholinyl, phenyl, pyrrolidinyl, pyridinyl, imidazolyl, imidazolyl-2-6C alkynyl, 1-6C alkylimidazolyl-2-6C alkynyl, cyanopyridinyl, phenyl-1-6C alkyl, phenyl-2-6C alkenyl, morpholinyl-1-6C alkyl, 1-6C alkyloxyphenyl, trihalo-1-6C alkylphenyl, methylpyrazolyl, halopyrimidinyl or dimethylaminopyrrolidinyl); aryl=phenyl or naphthalenyl; T2=thienyl, pyrrolyl, pyrazolyl, oxadiazolyl, piperidinyl, piperazinyl or pyridinyl; Het=T2, pyrrolinyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, tetrazolyl, thiadiazolyl, furanyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, azaindolizinyl, indolyl, indolinyl, benzothienyl, indazolyl, benzoxazolyl, benzimidazolyl, benzofuranyl, benzothiazolyl, benzotriazolyl, chromanyl, purinyl, quinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxazolinyl, naphthyridinyl or pteridinyl; R2=H, T1, 3-6C cycloalkyl, 3-6C cycloalkylmethyl, fluoro, phenyl or cyanophenyl; T1=methyl, ethyl, propyl or trifluoromethyl; R3=T1, hydroxymethyl, halo, methyloxy or 1-6C alkylcarbonyl; R4=H, halo, methyl, aminocarbonyl, hydroxyaminocarbonyl, NR8R9-1-6C alkyl-, cyanomethyl, hydroxymethyl or Het; R5 to R7=H, halo, 1-6C alkyloxy, cyano, 1-6C alkyl, -OCH2CH2NR8R9 , -CH2OCH2CH2NR8R9, -OCH2CH2CH2NR8R9 or 1-6C alkyloxy-1-6C alkyloxy; R8 and R9=H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, carbonyl, 1-6C alkylsulfonyl-1-6C alkyl, 1-6C alkyloxy-1-6C alkyl, hydroxy-1-6C alkyl, dihydroxy-1-6C alkyl, cyano-1-6C alkyl, trihalo-1-6C alkyl, phenyl-1-6C alkyl, (di-1-6C alkyl)amino-1-6C alkyl, 1-6C alkylsulfonyl, morpholinyl-1-6C alkyl, morpholinylcarbonyl, piperazinyl-1-6C alkyl, 1-6C alkylpiperazinyl-1-6C alkyl, piperidinyl-1-6C alkyl, thiomorpholinyl-1-6C alkyl, 3-6C cycloalkylmethyl, pyridinyl, pyrimidinyl, phenyl, halophenyl, oxanyl-1-6C alkyl, 1-6C alkylsulfonyl-1-6C alkyl or 1-6C alkylcarbonylamino-1-6C alkyl; R10 and R11=H, methyl or hydroxyl;or R10+R11=cyclopropyl ring or a radical of formula C(=O). INDEPENDENT CLAIMS are included for the following: (1) combination of the compound (I) with chemotherapeutic or anticancer agent; (2) preparation of the compound (I); (3) new intermediate of formula (II); and (4) preparation of the compound (II) involving either converting ketone group of intermediates of formula (III) into hydroxy group, with reductant, in a solvent, with formation of the compound (II) (where R3 is hydroxymethyl); or adding 2-methyl-2-propanol, potassium salt to intermediates of formula (V) in the presence of intermediates of formula R1-

(CH2)m-X-(CH2)n-Halo (VI), in a solvent, with formation of the compound (II) (where R3 is methyl, ethyl or propyl and R2 is methyl, ethyl, 3-6C cycloalkyl or phenyl); or adding 2-methyl-2-propanol, potassium salt to intermediates of formula (VII) in the presence of intermediates of formula R2-Halo, in a solvent, with formation of the compound (II) (where R3 is methyl, ethyl or propyl, and R2 is propyl or 3-6C cycloalkylmethyl). Halo=Cl or Br.

ACTIVITY - Cerebroprotective; Vasotropic; Cardiovascular-Gen.; Muscular-Gen.; Anti-HIV; Antiinflammatory; Antigout; Antiarthritic; Antiarteriosclerotic; Immunomodulator; Cytostatic; Antidiabetic; Cerebroprotective; Vulnerary; Gastrointestinal-Gen.; Osteopathic; Analgesic; Nephrotropic; Antibacterial; Immunosuppressive; Dermatological.

MECHANISM OF ACTION - Poly(ADP-ribose) polymerase (PARP) inhibitor; Tankyrase (TANK) inhibitor. The PARP-1 inhibitory efficacy of 3-(5-chloro-(1,2,3)thiadiazol-4-yl)-2-(3-ethyl-2-oxo-1,2- dihydro-quinolin-7-yl)-2-methyl-propionitrile (A1) was evaluated using in vitro scintillation proximity assay (SPA). The histones/poly(vinyl toluene) (PVT)-SPA beads solution and PARP-1 enzyme/DNA solution were mixed and 75 mu l of the mixture together with the compound (A1) (1 mu l) in dimethylsulfoxide (DMSO) and (3H)-NAD+ (25 mu l) was added per well into a 96-well microtiterplate. After incubation of the mixture for 20 minutes at room temperature, the reaction was terminated. The compound (A1) showed pIC50 value of 6.7.

USE - In the manufacture of a medicament for treating poly(ADP-ribose) polymerase (PARP) and tankyrase (TANK) mediated disorder, where treatment is chemosensitization or radiosensitization (claimed). Also for preventing or treating vascular stroke, cardiovascular disorders. For treating conditions and/or disorders such as age-related muscular degeneration, AIDS and other immune senescence diseases, inflammation, gout, arthritis, atherosclerosis, cachexia, cancer, degenerative diseases of skeletal muscle involving replicative senescence, diabetes, head trauma, inflammatory bowel disorders (such as colitis and Crohn's disease), muscular dystrophy, osteoarthritis, osteoporosis, neuropathic pain, renal failure, retinal ischemia, septic shock (such as endotoxic shock), and skin aging.

ADMINISTRATION - The dosage of the compound is 0.001-100 (preferably 0.005-10) mg/kg body weight, and is administered orally, rectally, percutaneously, or by parenteral injection.

ADVANTAGE - The compounds differ from the prior art as they have dual mode of action (PARP inhibition and tubulin binding); have high TANK inhibitory activity resulting in enhanced anti-cancer effects; and are also useful in enhancing effectiveness of chemotherapy and radiotherapy where primary effect of the treatment with the compound is that of triggering cell death under conditions of DNA damage.

EXAMPLE - Hydrochloric acid (3N, 1 ml) was added to a solution of 3-(5-chloro-(1,2,3)thiadiazol-4-yl)-2-(3-ethyl-2-methoxy-quinolin-7-yl)-2- methyl-propionitrile (0.0002 mol) in dioxane (3 ml). The mixture was stirred at 80 degrees C for 12 hours, poured out into ice water and basified with potassium carbonate. The organic layer was extracted with dichloromethane (DCM), dried, filtered and the solvent was evaporated. The residue was purified by column chromatography over silica gel. The pure fractions were collected and the solvent was evaporated. The residue was crystallized from diisopropyl ether. The precipitate was filtered off and dried, yielding 3-(5-chloro-(1,2,3)thiadiazol-4-yl)-2-(3-ethyl-2-oxo- 1,2-dihydro-quinolin-7-yl)-2-methyl-propionitrile (0.024 g, yield 28%) with melting point of 220 degrees C.(223 pages)

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 10:22:08 ON 08 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 6, 2009 (20090106/UP).

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=> d his ful

     (FILE 'HOME' ENTERED AT 09:10:01 ON 08 JAN 2009)

     FILE 'STNGUIDE' ENTERED AT 09:10:04 ON 08 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 09:10:21 ON 08 JAN 2009
                  ACT JAI086HCAAPP/A
                  ---------
L1             1 SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
                  ---------

     FILE 'WPIX' ENTERED AT 09:10:30 ON 08 JAN 2009
                  ACT JAI086WPIAPP/A
                  ---------
L2  (          2)SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
L3             1 SEA SPE=ON  ABB=ON  PLU=ON  L2 NOT AMUSEMENT/TI
                  ---------

     FILE 'REGISTRY' ENTERED AT 09:10:41 ON 08 JAN 2009
                  ACT JAI086REGAPP/A
                  ---------
L4  (          1)SEA SPE=ON  ABB=ON  PLU=ON  US2006-596086/APPS
L5               SEL PLU=ON  L4 1- RN :      48 TERMS
L6            48 SEA SPE=ON  ABB=ON  PLU=ON  L5
                  ---------
                  ACT JAI086PSET1/A
                  ---------
L7                STR
L8  (    1332204)SEA SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR NC2NC2-C6/ES
L9         22147 SEA SUB=L8 SSS FUL L7
                  ---------
                  ACT JAI086RSET1/A
                  ---------
L10               STR
L11 (    1332204)SEA SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR NC2NC2-C6/ES
L12 (      22147)SEA SUB=L11 SSS FUL L10
L13               STR
L14         1904 SEA SUB=L12 SSS FUL L13
                  ---------
                  ACT JAI086RSET2/A
                  ---------
L15               STR
L16 (    1332204)SEA SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR NC2NC2-C6/ES
L17 (      22147)SEA SUB=L16 SSS FUL L15
L18               STR
L19         1824 SEA SUB=L17 SSS FUL L18
                  ---------
                  ACT JAI086RSET3/A
                  ---------
L20               STR
L21 (    1332204)SEA SPE=ON  ABB=ON  PLU=ON  NC5-C6/ES OR NC2NC2-C6/ES
L22 (      22147)SEA SUB=L21 SSS FUL L20
L23               STR
L24 (       1824)SEA SUB=L22 SSS FUL L23
L25               STR
L26         1447 SEA SUB=L24 SSS FUL L25
                  ---------
L27           17 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND L6
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L28         1447 SEA SPE=ON  ABB=ON  PLU=ON  L26 NOT SEQUENCE/FS
L29         1446 SEA SPE=ON  ABB=ON  PLU=ON  L28 NOT PMS/CI
L30         1270 SEA SPE=ON  ABB=ON  PLU=ON  L29 NOT (S/ELS OR P/ELS OR SI/ELS)

L31            0 SEA SPE=ON  ABB=ON  PLU=ON  L27 NOT L30

     FILE 'STNGUIDE' ENTERED AT 09:14:50 ON 08 JAN 2009

     FILE 'ZCAPLUS' ENTERED AT 09:15:47 ON 08 JAN 2009
L32              QUE SPE=ON  ABB=ON  PLU=ON  MABIRE, D?/AU
L33              QUE SPE=ON  ABB=ON  PLU=ON  GUILLEMONT, J?/AU
L34              QUE SPE=ON  ABB=ON  PLU=ON  VAN DUN, J?/AU
L35              QUE SPE=ON  ABB=ON  PLU=ON  VANDUN, J?/AU
L36              QUE SPE=ON  ABB=ON  PLU=ON  SOMERS, M?/AU
L37              QUE SPE=ON  ABB=ON  PLU=ON  WOUTERS, W?/AU
L38              QUE SPE=ON  ABB=ON  PLU=ON  JANSSEN/CS,SO,PA
L39              QUE SPE=ON  ABB=ON  PLU=ON  AY<2006 OR PY<2006 OR PRY<2006 OR
                 MY<2006 OR REVIEW/DT

     FILE 'HCAPLUS' ENTERED AT 09:20:31 ON 08 JAN 2009
L40          114 SEA SPE=ON  ABB=ON  PLU=ON  L30
L41           11 SEA SPE=ON  ABB=ON  PLU=ON  L40 AND (L32 OR L33 OR L34 OR L35
                 OR L36 OR L37 OR L38)
L42          103 SEA SPE=ON  ABB=ON  PLU=ON  L40 NOT L41
L43           99 SEA SPE=ON  ABB=ON  PLU=ON  L42 AND L39

     FILE 'STNGUIDE' ENTERED AT 09:21:54 ON 08 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 09:22:39 ON 08 JAN 2009
L44           57 SEA SPE=ON  ABB=ON  PLU=ON  L40 (L)(BIOL+NT)/RL
L45            2 SEA SPE=ON  ABB=ON  PLU=ON  L27
L46           47 SEA SPE=ON  ABB=ON  PLU=ON  L42 AND (L44 OR L45)

     FILE 'REGISTRY' ENTERED AT 09:23:50 ON 08 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 09:23:53 ON 08 JAN 2009
L47              TRA PLU=ON  L46 1- RN :   16709 TERMS

     FILE 'REGISTRY' ENTERED AT 09:24:04 ON 08 JAN 2009
L48         16709 SEA SPE=ON  ABB=ON  PLU=ON  L47
L49           211 SEA SPE=ON  ABB=ON  PLU=ON  L30 AND L48
                 D QUE L26

     FILE 'LREGISTRY' ENTERED AT 09:26:33 ON 08 JAN 2009
L50              STR L25

     FILE 'REGISTRY' ENTERED AT 09:31:53 ON 08 JAN 2009
L51           50 SEA SUB=L26 SSS SAM L50
L52          368 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND (OC4/ES OR NC5/ES OR
                 NCNC2/ES OR N2CNC/ES)
L53          227 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND (NCNC2/ES OR N2CNC/ES)

     FILE 'HCAPLUS' ENTERED AT 09:38:30 ON 08 JAN 2009
L54           24 SEA SPE=ON  ABB=ON  PLU=ON  L53

     FILE 'REGISTRY' ENTERED AT 09:38:52 ON 08 JAN 2009
L*** DEL       0 S L26 AND ?PIPERIDIN?/CSN
L55           85 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND ?PIPERIDIN?/CNS
L56          311 SEA SPE=ON  ABB=ON  PLU=ON  (L53 OR L54 OR L55)
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     FILE 'HCAPLUS' ENTERED AT 09:40:50 ON 08 JAN 2009
L57            33 SEA SPE=ON  ABB=ON  PLU=ON  L56
L58            22 SEA SPE=ON  ABB=ON  PLU=ON  L42 AND (L27 OR L57)
L59             0 SEA SPE=ON  ABB=ON  PLU=ON  L58 AND (L32 OR L33 OR L34 OR L35
                  OR L36 OR L37 OR L38)
L60            22 SEA SPE=ON  ABB=ON  PLU=ON  L58 NOT L59
                  D BIB 22
L61            21 SEA SPE=ON  ABB=ON  PLU=ON  L60 AND L39

     FILE 'REGISTRY' ENTERED AT 09:43:07 ON 08 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 09:43:11 ON 08 JAN 2009
L62               TRA PLU=ON  L61 1- RN :    4659 TERMS

     FILE 'REGISTRY' ENTERED AT 09:43:16 ON 08 JAN 2009
L63          4659 SEA SPE=ON  ABB=ON  PLU=ON  L62
L64           118 SEA SPE=ON  ABB=ON  PLU=ON  L63 AND L56

     FILE 'LREGISTRY' ENTERED AT 09:44:55 ON 08 JAN 2009
                  D QUE L26
L65               STR L25

     FILE 'REGISTRY' ENTERED AT 09:45:29 ON 08 JAN 2009
L66            16 SEA SUB=L9 SSS SAM L65
                  D QUE STAT
L67           429 SEA SUB=L9 SSS FUL L65
                  SAVE TEMP L67 JAI086RSET5/A
L68           429 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND L67
L69             0 SEA SPE=ON  ABB=ON  PLU=ON  L27 NOT L68

     FILE 'HCAPLUS' ENTERED AT 09:49:25 ON 08 JAN 2009
L70            45 SEA SPE=ON  ABB=ON  PLU=ON  L67
L71             6 SEA SPE=ON  ABB=ON  PLU=ON  L70 AND (L32 OR L33 OR L34 OR L35
                  OR L36 OR L37 OR L38)
L72            39 SEA SPE=ON  ABB=ON  PLU=ON  L70 NOT L71
L73            36 SEA SPE=ON  ABB=ON  PLU=ON  L72 AND L39

     FILE 'REGISTRY' ENTERED AT 09:50:11 ON 08 JAN 2009

     FILE 'HCAPLUS' ENTERED AT 09:50:14 ON 08 JAN 2009
L74               TRA PLU=ON  L73 1- RN :    6661 TERMS

     FILE 'REGISTRY' ENTERED AT 09:50:20 ON 08 JAN 2009
L75          6661 SEA SPE=ON  ABB=ON  PLU=ON  L74
L76            46 SEA SPE=ON  ABB=ON  PLU=ON  L75 AND L67
                  D SCAN

     FILE 'WPIX' ENTERED AT 09:58:49 ON 08 JAN 2009
L77             0 SEA SSS SAM L65
L78            16 SEA SSS FUL L65
                  SAVE TEMP L78 JAI086WPIS/A
                  SELECT L78 1- SDCN
L79             7 SEA SPE=ON  ABB=ON  PLU=ON  (RACQIC/DCN OR RACQID/DCN OR
                  RACQIH/DCN OR RAI9EX/DCN OR RAI9EZ/DCN OR RAI9F0/DCN OR
                  RAJWHA/DCN OR RAMT44/DCN OR RA1G3S/DCN OR RA1G3T/DCN OR
                  RA1G3U/DCN OR RA1G3V/DCN OR RA1G3W/DCN OR RA56SN/DCN OR
                  RA56SP/DCN OR RA56U2/DCN) OR L78/DCR
L80             3 SEA SPE=ON  ABB=ON  PLU=ON  L79 AND (L32 OR L33 OR L34 OR L35
                  OR L36 OR L37 OR L38)
L81             4 SEA SPE=ON  ABB=ON  PLU=ON  L79 NOT L80
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                D BIB HITSTR 1-4

     FILE 'STNGUIDE' ENTERED AT 10:02:38 ON 08 JAN 2009

     FILE 'MEDLINE, BIOSIS, EMBASE, CABA, BIOTECHNO, DRUGU, VETU, AGRICOLA'
     ENTERED AT 10:03:06 ON 08 JAN 2009
L82             0 SEA SPE=ON  ABB=ON  PLU=ON  L67

     FILE 'STNGUIDE' ENTERED AT 10:03:38 ON 08 JAN 2009

     FILE 'ZCAPLUS' ENTERED AT 10:08:55 ON 08 JAN 2009
L83             QUE SPE=ON  ABB=ON  PLU=ON  ?QUINOLINON? OR ?QUINOXALINON?
L84             QUE SPE=ON  ABB=ON  PLU=ON  ADP
L85             QUE SPE=ON  ABB=ON  PLU=ON  POLYMERAS?

     FILE 'MEDLINE, BIOSIS, EMBASE, PASCAL, CABA, CEABA-VTB, LIFESCI, BIOENG,
     BIOTECHNO, BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI,
     DISSABS, RDISCLOSURE' ENTERED AT 10:10:59 ON 08 JAN 2009
L86           273 SEA SPE=ON  ABB=ON  PLU=ON  L83 AND L84 AND L85
L87             1 SEA SPE=ON  ABB=ON  PLU=ON  L86 AND (L32 OR L33 OR L34 OR L35
                OR L36 OR L37 OR L38)
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 10:12:06 ON 08 JAN 2009
                D SAVED
                D QUE STAT L9
                D QUE STAT L14
                D QUE STAT L19
                D QUE STAT L26
                D QUE STAT L67
                D QUE NOS L72
                D QUE STAT L78
                D QUE L81
                D QUE NOS L82

     FILE 'HCAPLUS, WPIX' ENTERED AT 10:15:37 ON 08 JAN 2009
L88            42 DUP REM L72 L81 L82 (1 DUPLICATE REMOVED)
                     ANSWERS '1-39' FROM FILE HCAPLUS
                     ANSWERS '40-42' FROM FILE WPIX
                SAVE TEMP L88 JAI086MAIN/A

     FILE 'STNGUIDE' ENTERED AT 10:15:52 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX' ENTERED AT 10:16:10 ON 08 JAN 2009
                D IBIB ED ABS HITIND HITSTR 1-20

     FILE 'STNGUIDE' ENTERED AT 10:16:21 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX' ENTERED AT 10:18:13 ON 08 JAN 2009
                D IBIB ED ABS HITIND HITSTR 21-39

     FILE 'STNGUIDE' ENTERED AT 10:18:25 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX' ENTERED AT 10:18:51 ON 08 JAN 2009
                D IALL ABEQ TECH ABEX HITSTR 40-42

     FILE 'STNGUIDE' ENTERED AT 10:18:57 ON 08 JAN 2009
                D QUE NOS L71
                D QUE L80
                D QUE NOS L82
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             D QUE L87

     FILE 'HCAPLUS, WPIX, BIOTECHDS' ENTERED AT 10:20:02 ON 08 JAN 2009
L89          9 DUP REM L71 L80 L82 L87 (1 DUPLICATE REMOVED)
                  ANSWERS '1-6' FROM FILE HCAPLUS
                  ANSWERS '7-8' FROM FILE WPIX
                  ANSWER '9' FROM FILE BIOTECHDS
             SAVE TEMP L89 JAI086INV/A

     FILE 'STNGUIDE' ENTERED AT 10:20:16 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX, BIOTECHDS' ENTERED AT 10:20:38 ON 08 JAN 2009
             D IBIB ED ABS HITIND HITSTR 1-6

     FILE 'STNGUIDE' ENTERED AT 10:20:45 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX, BIOTECHDS' ENTERED AT 10:21:26 ON 08 JAN 2009
             D IALL ABEQ TECH ABEX HITSTR 7-8

     FILE 'STNGUIDE' ENTERED AT 10:21:31 ON 08 JAN 2009

     FILE 'HCAPLUS, WPIX, BIOTECHDS' ENTERED AT 10:21:58 ON 08 JAN 2009
             D IBIB ED AB 9

     FILE 'STNGUIDE' ENTERED AT 10:22:03 ON 08 JAN 2009

     FILE 'STNGUIDE' ENTERED AT 10:22:08 ON 08 JAN 2009


     FILE HOME

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
     LAST RELOADED: Jan  6, 2009 (20090106/UP).

     FILE HCAPLUS

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      This file contains CAS Registry Numbers for easy and accurate
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     FILE WPIX
     FILE LAST UPDATED:          3 JAN 2009   <20090103/UP>
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FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE MEDLINE
FILE LAST UPDATED: 7 Jan 2009 (20090107/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Libra of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

MEDLINE Accession Numbers (ANs) for records from 1950-1977 have been converted from 8 to 10 digits. Searches using an 8 or 10 digit AN will retrieve the same record. The 10-digit ANs can be expanded, searched, and displayed in all records from 1949 to the present.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 7 January 2009 (20090107/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE
FILE COVERS 1974 TO 7 Jan 2009 (20090107/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE

codes.

For further assistance, please contact your local helpdesk.

FILE CABA
FILE COVERS 1973 TO 5 Dec 2008 (20081205/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

The CABA file was reloaded 7 December 2003. Enter HELP RLOAD for details.

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.
THIS FILE IS A STATIC FILE WITH NO UPDATES

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
/CT AND BASIC INDEX <<<

FILE DRUGU
FILE LAST UPDATED: 7 JAN 2009 <20090107/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE VETU
FILE LAST UPDATED: 2 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE AGRICOLA

FILE COVERS 1970 TO 6 Jan 2009 (20090106/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE PASCAL
FILE LAST UPDATED: 22 DEC 2008 <20081222/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

FILE CEABA-VTB
FILE LAST UPDATED: 12 DEC 2008 <20081212/UP>
FILE COVERS 1966 TO DATE

>>> DECHEMA, the producer of CEABA-VTB is using a new classification
scheme.
The new classification schemes are available as a PDF file
and may be downloaded free-of-charge from:

http://www.stn-international.de/news/cc-de.pdf
and
http://www.stn-international.de/news/cc-en.pdf <<<

FILE LIFESCI
FILE COVERS 1978 TO 30 Dec 2008 (20081230/ED)

FILE BIOENG
FILE LAST UPDATED: 2 JAN 2009 <20090102/UP>
FILE COVERS 1982 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
THE BASIC INDEX <<<

FILE BIOTECHDS
FILE LAST UPDATED: 23 DEC 2008 <20081223/UP>
FILE COVERS 1982 TO DATE

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

FILE DRUGB
>>> FILE COVERS 1964 TO 1982 - CLOSED FILE <<<

FILE VETB
FILE LAST UPDATED: 25 SEP 94 <940925/UP>
FILE COVERS 1968-1982

FILE SCISEARCH

FILE COVERS 1974 TO 1 Jan 2009 (20090101/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE CONFSCI
FILE COVERS 1973 TO 6 Nov 2008 (20081106/ED)

CSA has resumed updates, see NEWS FILE

FILE DISSABS
FILE COVERS 1861 TO 5 DEC 2008 (20081205/ED)

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FILE RDISCLOSURE
FILE LAST UPDATED: 10 DEC 2008 <20081210/UP>
FILE COVERS 1960 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE
BASIC INDEX (/BI) AND TITLE (/TI) FIELDS <<<

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